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The Journal of Laboratory and Clinical Medicine

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ORIGINAL ARTICLES

ENCEPHALITIS LETHARGICA

BY VICTOR C. VAUGHAN, M.D., ANN ARBOR, MICH.

NEWSPAPER reporters are now busy interviewing the doctors concerning the new disease popularly known as "sleeping sickness." In my opinion, any real information on this subject should be given to the newspapers. The time has long since passed when knowledge concerning disease, and especially epidemic disease, should be withheld from the public. The better newspapers in the country now go to the best doctors for information along these lines, rather than, as formerly, to quack nostrum venders. The wise physician uses every legitimate effort to educate the public, and the agency through which this can be best accomplished is the reputable newspaper which constitutes the most important agent for the diffusion of knowledge among the masses. Even the most alert and up-to-date physician knows little about this disease, and the purpose of this writing is to gather together and make available to the profession the more technical details concerning it. I learn from the English review of the foreign medical press that a monograph on encephalitis lethargica has been published at Vienna by Professor Economo. I have not seen this monograph, and herewith introduce the greater part of the notice as it appears in the English review. The statement is as follows:

"In this monograph Economo has republished in readable form the results of his investigations into the epidemic of infective encephalitis, which occurred in Vienna in the winter of 1916-17 without adding much to our knowledge of this interesting disease. Details of thirteen excellently described clinical cases (two of which are new) are given. Of these thirteen cases, five died and were examined both macroscopically and microscopically after autopsy. In all cases the Wasser-

mann reaction in both blood and cerebrospinal fluid was negative (difference from poliomyelitis), and all were tested serologically against various strains of the Bacillus typhosus. The infective encephalitis of man can be conveyed to apes. The cause of the illness, according to the author, can neither be a toxin nor a poison, but must be due to a living organism. This organism can not pass through a Berkefeld filter, and in this respect differs entirely from the organism of poliomyelitis (Heine-Medin disease). From an infected ape a pure culture of a diplostreptococcus was obtained by von Wiesner. This organism when injected into animals produces in those animals a hemorrhagic encephalitis; in some instances in man the encephalitis has also shown hemorrhagic characters. The author discusses adequately the various symptoms; the mode of onset, the fever, the delirium, the somnolence (which he attributes to the localization of the pathologic lesions in the neighborhood of the optic thalamus), the meningismus, the changes in the cerebrospinal fluid, blood, urine, the ocular symptoms, the signs of bulbar interference, the palsies of the extremities, rigidity, athetosis, ataxy. No known measures of therapy have influenced the course of the disease. Excellent descriptions of the changes found in the central nervous system in cases which have died in the active and in more quiescent stages of the infection are given. The descriptions are illustrated by 12 drawings. The author is of opinion that infective encephalitis is pathologically an inflammation of the parenchyma of the central nervous system, complicated by a secondary small-celled infiltration of the vessels.

"A comparison of the lesions found at autopsy, with the findings in cases of dementia paralytica, sleeping sickness, rabies, poliomyelitis, the Borna disease of horses and acute multiple sclerosis, is made and the conclusion reached that infective encephalitis differs from all these. And, finally, it is stated that 'the infective polioencephalitis lethargica is a disease which may assume an epidemic form (as Nona, as the Tübingen sleeping sickness, and perhaps as Morbus Guerlier and as in Vienna) just as can poliomyelitis, but that sporadic cases are always turning up, and that the disease is due to the earlier described diplostreptococcus.'"

We learn from the Lancet of January 11 that the disease has been made reportable in England. A recurrence this spring is predicted. The suggestion that the disease might be due to food infected with the Bacillus botulinus has been investigated by the local government board with a negative conclusion. The same board has reached the decision that this disease is not anterior poliomyelitis, but is a disease *sui generis* of unknown causation. It belongs to the class of polioencephalitic diseases which are inflammatory in nature, but the inquiry has not yielded any conclusive evidence as to the character of the causal agent. When it is considered that the organism which causes the analogous disease, poliomyelitis, is still a matter for debate, although thousands of cases have been investigated from the bacteriologic point of view, it is not surprising that the problem of the causal agent of encephalitis lethargica is as yet unsolved.

McNalty suggests that the relation of this disease to anterior poliomyelitis may be similar to that of paratyphoid to typhoid. He also stresses the influence of lowered resistance, due to war conditions, as a result of which a saprophytic organism may become pathogenic. According to James, this idea is further

strengthened by the widely scattered and sporadic prevalence of the disease. Marinesco and McIntosh emphasize the similarity of the lesions with those of anterior poliomyelitis, especially in the cellular infiltration around the smaller veins in the basal ganglia, the upper part of the pons, particularly in the gray matter of the floor of the fourth ventricle, and to a much less degree in the medulla. Both failed to find evidence of a specific organism, and inoculations of monkeys were without effect.

On May 5, 1918, Netter gave a most interesting paper on this disease before the Paris Academy of Medicine. About two months earlier many cases were seen in the hospitals and in private practice in Paris. The striking symptoms were somnolence, drooping of the upper eyelids, accompanied by mild fever. Though meningitis was the first diagnosis, its characteristic symptoms,—Kernig's sign, rigidity and irregularity of the pulse—were wanting or in doubt. Lumbar puncture yielded normal fluid with no increased pressure. The disease continued for weeks and about 50 per cent of the infected individuals died. Macroscopically there were congestion of the meninges and scattered hemorrhages in both the gray and white matter. Microscopic examination showed cellular infiltration, especially marked about the blood vessels. The lesions were most numerous and most marked in the medulla, pons, and basal nuclei of the brain. Netter regards the disease as an encephalitis of unknown causation, and recalls the fact that under the name "Nona" such a disease was reported in the spring of 1890, especially in Northern Italy and Hungary, but here and there over a large part of Europe. As early as 1712 a similar disease following a pandemic of influenza was reported in Germany and locally known as "Tübingen sleeping sickness." Recently, this disease was first reported at Vienna in the winter of 1916-17. Netter rejects the idea that this disease is anterior poliomyelitis. Lethargic encephalitis, he says, is a disease of winter and spring, while anterior poliomyelitis prevails in summer. The former is much more common in adults, although no age is absolutely exempt. In both, interstitial encephalitis is found, but the involvement of the ganglionic cells, so pronounced in poliomyelitis, is slight in lethargic encephalitis. He also rejects the idea that it is a form of botulism, because if this were the case, it should appear among those who eat at the same mess, whereas multiple cases of the new disease in the same household have not been seen.

Batton and Still (Lancet, London, 1918, i, 636) report an epidemic stupor in children. The report covers four cases, aged three and one-half months, four, seven, and eleven years. The stupor developed rapidly without convulsions, though in one case it was preceded by a listless state. All were brought to the hospital in a state of stupor with the eyes closed, the legs extended, and the arms sometimes flexed, sometimes extended. There was general rigidity of the muscles, but the limbs could be placed in any position and then showed a tendency to remain where placed—a cataleptic state. Although apparently unconscious, they could be aroused and then they slowly responded to inquiries. When asked to open their eyes there was a flickering movement through the muscles before the act was accomplished. When the lids were lifted passively, the eyes were found to be divergent. All swallowed normally, and even when in apparent stupor took readily of the food brought to their lips. The babe nursed when

placed at the mother's breast. At first there was a slight elevation of temperature, but this passed in a few days, while the stupor continued for weeks. The respirations were normal and the pulse regular except in one case which showed some irregularity. The reflexes, both superficial and deep, were normal. The cerebrospinal fluid flowed under normal pressure and revealed no abnormality. The blood showed no abnormal condition, and the Wassermann test was negative. After from three to five weeks the stuporous condition gradually passed away. No two of the children were from the same family, and no other member of any of the families presented similar symptoms. The babe had had no other food than that drawn from its mother's breast, and so far as could be determined, she was in health. An anonymous writer (Lancet, London, 1918, i, 715) commenting on the above report, thinks that the cases have been reported too soon; that the children will not fully recover but will die and autopsy will show either tuberculous or pneumococcal meningitis.

McCaw, Perdran and Stibbing (Lancet, London, 1918, i, 616) report six cases under the diagnosis of toxic bulbar paralysis, and attribute the same to botulism. These cases seem to differ in some details from those reported by others. In two, the spinal fluid flowed with increased pressure. In one, the antemortem temperature reached 109.° There was no evidence of meningitis, and the only detectable lesion was slight edema with some congestion of the floor of the fourth ventricle. The same condition is reported in the three fatal cases. Microscopic studies had not been made at the time of the publication of the report.

Harris (Lancet, London, 1918, i, 568) under the diagnosis of botulism reports six cases. One of these was most probably a case of true botulism. This man ate sausage in the morning and lobster for lunch and spent the night in vomiting. After this he was drowsy, developed bilateral ptosis with divergent strabismus, inability to swallow, and retention of urine. An organism "resembling the Bacillus botulinus" was found in the stools and urine.

The first official report of this disease in England seems to have been made January 26, 1918. Most of the cases so far reported have been in London, but there have been cases scattered all over England and Wales. In only one instance have there been two cases, and one of these was mild and of doubtful diagnosis, in the same family.

Porthier (Jour. Am. Med. Assn., 1919, lxxii, 715) reports eight cases of this disease from Camp Lee in Virginia, with one death. In the fatal case autopsy showed no marked abnormality in the cord. In the brain, the following is a statement of the findings:

"On section of the hemispheres, the centrum ovale presented dilatation of the blood vessels, which appeared as small, punctate bodies throughout the surface. On inspection, the corpus callosum appeared normal; but on attempt to section, it was found to be soft and mushy. All the tissues of the lateral ventricles were soft. The optic thalamus was softened. The velum interpositum and the chorioid plexus presented the same condition as the vessels of the surface of the brain; that is, the vessels were prominent, tortuous and arborescent. There was no excess of fluid in the ventricles, but all the tissues surrounding them were softened, the brain substance as well as the tissues of the floor. The third ventricle presented nothing of note, except general softening of the tis-

sues of the floor. The pineal gland was swollen. The iter a tertio ad quartum was patulous. On section of the basal ganglions a small hemorrhagic spot was found in the right hemisphere immediately adjoining the internal capsule. This spot was about 1 mm. in diameter. On the left side, the basal ganglions presented nothing of note. Anteroposterior sections through the hemispheres presented nothing of note. Sections through the cerebellum presented nothing of note. There was, however, a universal softening of the brain tissue which made it very hard to section without destroying it in the attempt. After sectioning, the organ was apparently collapsed, and there was no possibility of returning the sectioned portion back to the former relation on account of this softening."

The several patients came from widely separated organizations in the camp. The chief symptoms were vertigo, diplopia, headache, slight fever, and the spinal fluid showed a definite pleocytosis (from 20 to 66 cells) of the lymphocytic type.

Wilson (Lancet, London, July 6, 1918) states that the general symptoms are apathy, lethargy, drowsiness, and absence of initiative. In some instances there may be marked restlessness, alternating with profound indifference. Delusions and hallucinations may be manifest. The temperature may be either above or below normal. Paralysis of accommodation with indistinct vision is an early symptom. The drooping of the eyelids may be bilateral or unilateral. The facies is often expressionless with obliteration of the lines on account of a bilateral paralysis. The affection of the cranial nerves is motor, and not sensory. Rarely the limbs are involved, but this is due to disturbance in the cortical paths and not to invasion or involvement of the cord. The spinal fluid is usually normal and pleocytosis is the exception and occurs only when the meninges are involved. This author gives the points of differentiation from poliomyelitis, some of which are as follows:

1. In the latter disease, the lethargic element is wanting.
2. Lethargic encephalitis is most frequent in winter; poliomyelitis in summer.
3. The former is more common in adults; the latter, in children.
4. In encephalitis lethargica the spinal fluid is normal.
5. Meningeal symptoms are more frequent in poliomyelitis.
6. Two or more cases in the same family have not been seen in lethargic encephalitis but is a common observation in poliomyelitis.

In botulism there are no inflammatory lesions in the brain. This is an anatomic condition, and of course can be discerned only at autopsy. Drooping of the eyelids is the most common sign in encephalitis lethargica and is present in at least 75 per cent of the cases.

McNalty distinguishes seven types of the disease. These are as follows:

1. The affection is limited to the third pair of cranial nerves.
2. The brain stem and the bulb are involved.
3. The chief affection is in the long tracts.
4. There is an ataxic type.
5. The cerebral cortex is the chief center of the involvement.
6. There may be signs and evidence of spinal cord involvement.
7. The polyneuritic type.

In England during the spring of 1918, there were 168 officially reported cases, with 37 deaths. The disease seems to have disappeared in June, 1918, but reappeared in the fall of that year.

It must be evident that the time has not come when anything but tentative statements can be made concerning this disease. From the literature, we gather that it is a disease principally involving the brain itself; that there is in many cases more or less involvement of the meninges but this is not prominent. In no case is the cord involved. The stupor is partly apparent and partly real. The real stupor is due to the cerebral involvement. The apparent stupor is due to partial paralysis of the motor nerves employed in lifting the upper eyelids. Coma is not a symptom of the disease.

It is more than probable that a great variety of conditions will be reported as encephalitis lethargica. Already it has come to my knowledge that claims are being made for special treatment in this disease by persons who have never seen it. Only a few days ago, a masseur wrote that she had frequently treated this disease with the best results in the southern states, and that it had followed typhoid fever. There is no authentic case on record in which this disease has followed typhoid. Is it a sequela to influenza? The only reason, and it is a good one, for suspecting that such is the case is that in the past it has followed a pandemic of influenza. To say that one has not had influenza does not mean that influenza is not an essential forerunner of the disease. Most people who have lived through epidemics of influenza, even when there has been no recognizable appearance of the disease in them, have acquired at least a temporary immunity to influenza. The natural conclusion to draw from this is that in a large number —indeed in the majority of people in the midst of an epidemic of influenza— the virus affects the people sufficiently to give a temporary immunity, and it may be that the virus of influenza without causing recognizable acute symptoms may after weeks or months produce the changes in the brain observed in encephalitis lethargica.

EPIDEMIC CEREBROSPINAL MENINGITIS AT CAMP CODY*

By Frederick H. Lamb, M.D.
Captain, M.C., Chief of Laboratory Service, Base Hospital, Camp Cody, Deming, N. M.

DURING the winter of 1917-18, the occurrence of epidemic cerebrospinal fever in many, if not in all, of the army and navy cantonments was a source of considerable apprehension for all concerned. Long before the discovery of the meningococcus, epidemic meningitis was known to be a serious menace to the armed camp. It was dreaded especially in camps of new, unseasoned recruits.

True to form, meningitis appeared in the European armies promptly after their mobilization in the present war. It became a very serious problem in some of them. Medical officers predicted with certainty that the disease would appear in our own forces, which it did just as soon as any considerable number of recruits were assembled in close quarters. It could not be foretold how extensively or how rapidly the disease would spread within camps, nor was it known whether an epidemic could be thwarted or controlled among such large numbers.

According to a report of communicable diseases in the army by Vaughan and Palmer,[1] Camp Jackson, South Carolina, Camp Beauregard, Louisiana, and Camp Funston, Kansas, suffered most heavily among the army camps, from meningitis (all forms were included in their report.) I was stationed at Camp Funston during the months of November, December, 1917, and January, 1918, and can certify that the epidemic of meningitis there was, next to pneumonia, the most serious medical problem of the camp. On account of quarantine, isolation of carriers, and sanitary measures instituted against the spread of the epidemic, it caused a much greater dislocation of training activities than did pneumonia.

Early in February, 1918, Camp Cody seemed to be threatened with a similar experience. Two cases of meningococcus meningitis had developed in December, 1917, and three in January, 1918. Four cases developed during the first ten days of February. During January some troops were transferred here from Camp Funston where the percentage of carriers had been found to be high. Another factor deserving consideration at that time, was the question of the influence of the sand and dust storms which are prevalent at this camp during the winter and spring. Many cases of chronic, low-grade rhinitis and pharyngitis were attributed to this cause, and that such a condition of the nasopharyngeal mucosæ might favor the growth of meningococci was regarded as a possibility. The combination of these various circumstances was somewhat alarming.

QUARANTINE MEASURES

Realizing the possibility of a serious outbreak, stringent measures were taken to safeguard the command against the spread of the disease. Organization surgeons were directed to be on the alert for symptoms, however mild, of meningitis, attention being called to the extreme importance of early diagnosis and

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treatment. In order to unify the preventive measures, a circular letter was sent to each surgeon, setting forth both general and specific directions to be followed regarding quarantine, reports, and the culturing of organizations for the detection of carriers. The following extract from the letter of instruction indicates the specific procedure to be followed in organizations developing a case of meningitis:

1. Strict quarantine will be maintained until the company or unit is released by a report of cultures for carriers.

2. The contact squad will be confined under guard during the time, and food brought to it.

3. In order to sun and air clothing and bedding, tents will be furled every day, weather permitting, from 8:00 A.M to 4:00 P.M..

4. The equipment and effects of meningitis patients and carriers will be sterilized, and the premises scrubbed with antiseptics.

5. Washing of hands before meals will be done under military supervision.

6. Each man will immerse his eating utensils in boiling water both before and after meals.

7. Paper napkins will be used in place of handkerchiefs and will be burned as soon as soiled.

8. Wash and boil all soiled linen at once.

9. Avoid all indoor meetings.

10. Medical officers will assemble companies in the streets and talk to them emphasizing the fact that the disease is spread by carriers by means of coughing, sneezing, spitting and the use of articles in common.

11. The following articles are often used by soldiers promiscuously: roller and hand towels, soap, brushes and combs, canteens, drinking cups, pipes, whistles, musical instruments, playing cards and dice.

12. The interchanging of clothing or sleeping upon the cots of others is forbidden.

While the above measures were regarded as being important, yet it was fully realized that the greatest hope of preventing an epidemic of meningitis lay in the detection and elimination of carriers. So far as is known, the meningococcus gains entrance to the body through the nasopharyngeal mucosæ. It escapes with the secretions and excretions from the nose and mouth. Consequently, the bacteriologic control of an epidemic centers upon these membranes.[2]

PRACTICAL DIFFICULTIES OF AN EXTENSIVE SURVEY

Theoretically, the detection of all meningococcus carriers, in a military organization of limited size is quite feasible. Practically, it is a difficult undertaking in a large army cantonment. For instance, a well-trained bacteriologist with a corps of experienced technicians and a thoroughly well equipped laboratory should be able to detect and control, with a considerable degree of accuracy, the meningococcus carriers in a unit numbering 1,000. Frequent reculturing of the entire unit is, in my opinion, essential. Suspicious or actual carriers should be isolated. Cultures should be taken from carriers daily until at least five consecutive negatives have been obtained before they return to the unit. These individuals should thereafter have cultures made at least once each week.

Swabbings should be made from the anterior nares by means of a nasal speculum and cotton-tipped applicators; also from the nasopharynx by means of West tubes. Cultures should be made in a warm room, carefully spread over warm culture plates, and placed at once in an incubator. Every known refinement in technic, from the making of culture medium to the last step in identifying organisms by well controlled agglutination tests, should be practiced. Several plates inoculated with recently isolated strains of meningococci (on account of their weak viability in contrast to that of old cultures) should be incubated with each batch of plates to serve as controls of the medium, incubation, identification of colonies, staining and agglutination. The drudgery incident to such routine and detail should never be allowed to cause relaxation of effort. Eternal vigilance under ideal conditions is the price of freedom from meningococcus carriers.

Such conditions are almost impossible to attain in a large army cantonment numbering upward of 20,000 individuals. The taking of cultures is a time-consuming process. Naturally, it interferes with the already crowded schedule of military training, which is the primary and most important function of the camp. Even with the hearty cooperation of commanding officers it is often not possible to culture an entire unit. Some members are usually on sick report, on furlough, or on special detail from which their services can not be spared. The result is that there are usually several soldiers in each company from whom cultures are not obtained, and any one of these may be a carrier. The transfer of enlisted men from one unit to another, which is unavoidable at times; also the introduction of recruits from other camps to organizations which have been cultured, make it necessary to culture "stragglers" at odd times. But in any case the system is not "air-tight."

To repeat: a large, well-trained, highly efficient laboratory force is essential to such an undertaking. Last winter it was impossible to supply such a force to each camp.

Notwithstanding these and other minor factors which militated against a perfect survey, it was decided to make the best use of all available means to culture the entire personnel of the camp, hoping thereby to eliminate most of the carriers. A contact camp was established for the isolation and treatment of carriers. The culturing of organizations, in which cases of meningitis had developed, was begun February 6, 1918, with others following as rapidly as possible.

For two good reasons it was considered advisable to take all cultures in the laboratory, rather than in the camp, as had been the practice at Camp Funston. The short distance between the camp and the hospital rendered it possible to march soldiers to the hospital with but little loss of time. The culture plates could, with greater certainty, be kept warm, and free from contamination. (The latter had always been a vexing problem in this camp on account of the sand storms.) Nasopharyngeal cultures, by means of West tubes, were taken by a medical officer with the help of a clerk and technician. In a short time, this team became very efficient so that as many as 900 cultures could be taken in a morning, although a daily average of from 500 to 600 cultures was found to be the optimum.

TECHNIC

The laboratory technic followed was essentially that laid down at the Rockefeller Institute. Veal infusion 2.5 per cent agar, adjusted to a reaction of +0.3 phenolphthalein, was prepared in large quantities, autoclaved and stored in bottles containing about 300 c.c. As many of these as were required for the day's work were melted, 20 c.c. of sterile 20 per cent dextrose solution added, and cooled to 50 degrees C. To this was added 80 c.c. of laked blood, prepared by adding 20 c.c. of defibrinated human blood to 60 c.c. of distilled water. In bulk this medium was a clear, cherry red color. From 8 to 10 c.c. quantities were poured into sterile Petri dishes, care being taken to tilt and shake the dish immediately after pouring, so that an even film of medium 2 to 3 mm. thick, covered the bottom. To insure sterility, the plates were incubated twenty-four hours before use.

During the culturing process, the plates were removed from one incubator, inoculated, labeled and immediately placed in another incubator. After twenty to twenty-four hours incubation they were examined for meningococcus colonies. Suspicious colonies were circled with a wax pencil. Where the colony was large enough a part of it was "fished," spread on a slide, stained, and examined in order to determine, at once, the Gram reaction of the organism. This could be done rapidly by placing from 16 to 24 colony-specimens on a slide in order to stain all of them at once. In this way, colonies in which no Gram-negative cocci appeared could be safely discarded. Very small colonies, and those showing Gram-negative cocci were transplanted to serum (human or horse) dextrose agar slants. After twenty-four hours' incubation, the surface of these slants was washed down with 0.8 per cent salt solution and suspension made for the agglutination tests. At this point it may be well to emphasize the observation which has been made regarding the peculiar tendency of pure meningococcic cultures to form a very fine suspension with very little agitation. Cultures of other organisms, especially cocci, required a great deal more shaking in order to get anything like a fine, even suspension. The agglutination tests were carried out in small serologic test tubes, at a temperature of 55° for twenty to twenty-four hours, using 1:50 and 1:200 dilutions of both Rockefeller polyvalent and New York State Board immune sera, and controlled by normal horse serum and salt solution. It was found very helpful in the final decision as to whether an organism was the meningococcus or not, to refer to a table in which the following points were noted: character of the colony, Gram reaction, morphology, emulsifying properties, and agglutination reaction. It is believed that many false positives were in this way avoided.

Throughout the survey, all records and data were kept by a system of dates and numbers. The date was written on the cover of the Petri dish; the numbers of the cultures on the bottom. For instance, 2/15—10 meant the tenth culture taken February 15. This culture could be identified only by reference to the roster in which was recorded the soldier's name and organization. In this way, reports were made without any reference to organization. It is interesting to note in Table I, showing the final reports by organization, the fairly uniform percentage of carriers.

TABLE I

SHOWING THE NUMBER OF CULTURES, CARRIERS, PERCENTAGE OF CARRIERS AND NUMBER OF CASES BY ORGANIZATIONS

ORGANIZATION	NUMBER OF CULTURES	NUMBER OF CARRIERS	PER CENT OF CARRIERS	TOTAL NUMBER OF CASES	NUMBER OF CASES IN FEB., 1918
133 Infantry	2,038	37	1.81	2	1
134 Infantry	2,541	33	1.29	1	1
135 Infantry	2,665	29	1.08	2	2
136 Infantry	2,921	38	1.30	3	2
125 Field Artillery	1,021	10	0.97	1	1
126 Field Artillery	1,254	10	0.79	1	1
127 Field Artillery	1,197	13	1.08	1	–
126 Machine Gun Bn.	648	10	1.54	2	2
127 Machine Gun Bn.	635	4	0.62	1	1
109 Engineer Train	583	9	1.54	–	–
109 Ammunition Train	880	12	1.36	–	–
109 Sanitary Train	793	5	0.63	1	–
109 Supply Train	244	8	3.27	1	–
109 Field Signal Bn.	408	4	0.98	–	–
Base Hospital Med. Det.	382	5	1.30	–	–
Division Stockade	103	2	1.94	–	–
Recruits	530	9	1.69	–	–
Miscellaneous, including small organizations, "stragglers," civilians, etc.	1,365	21	1.53	–	–
	20,208	259	1.28 (Average)	16	11

CARRIERS

The percentage of carriers in the total of 20,208 cultures (representing between 90 and 95 per cent of the strength of the command) was 1.28 per cent.

Carriers were sent, immediately after their detection, to the Isolation Camp, which was in charge of a medical officer, and where strict attention was given to personal and camp hygiene. Each carrier received a nasopharyngeal spray of 2 per cent dichloramine-T oil four times daily, and was sent to the laboratory every fourth day for reculturing. The carrier was allowed to return to his respective unit when three consecutive negative cultures had been obtained.

TABLE II

SHOWS THE NUMBER OF DAYS IN ISOLATION REQUIRED TO GET THREE NEGATIVE CULTURES AT FOUR-DAY INTERVALS

12 days	16 days	20 days	24 days	28 days	32 days	36 days	40 days	Over 40 days
171	18	14	4	6	7	7	4	5

The reculture records of 236 of the 259 carriers are complete. Table II shows the number of days in isolation required to get three negative cultures at four-day intervals. It does not, however, represent the actual carried period, since all carriers were held twelve days after the last positive culture. In many

instances a positive culture would be found after 1 or 2 negatives. Of a total of 1,161 cultures from the Isolation Camp, 89 or 7.6 per cent were positive, which was six times that of the camp.

CASES

As stated before, two cases of epidemic meningitis occurred in December, 1917, and three in January, 1918; two of the five terminating fatally. During February, seventeen cases were admitted to the Base Hospital with a tentative diagnosis of epidemic meningitis. In five of these the spinal fluid findings did not substantiate the diagnosis of meningitis. Of the remaining twelve, one proved to be a streptococcic meningitis following otitis media. Eleven were regarded as epidemic meningitis, and so treated, although the meningococcus was found in but eight. The organism was recovered from blood culture in one case.

Clinically, these cases as a group presented nothing very remarkable. Two were very severe, the others, if anything, rather mild. Erythematous spots were observed in but one case although carefully watched for in all. None of the cases of this series died. Regarding the ultimate military disposition, one patient was discharged from the army upon a surgeon's certificate of disability. Two others were transferred to another hospital; eight were returned to duty.

The specific treatment, to which a very great measure of the credit is due, consisted of both intraspinal and intravenous administrations of antimeningococcic serum. Both the Rockefeller polyvalent and New York State Board sera were used. Large doses were given as often as four times in twenty-four hours, although twice a day was the rule.

REPORT OF A CASE

One case is worthy of mention, chiefly on account of the complications and sequelæ which developed:

Case I. Wagoner E. L. B., 126 M. G. Bn., was admitted to the Base Hospital, February 7, 1918, complaining of general bodily aching, chills, and severe headache. Ten c.c. of clear cerebrospinal fluid, under slightly increased pressure, were withdrawn. After a long search, several Gram-negative, extracellular, diplococci were found in the centrifuged sediment. Another specimen taken the following day, was very turbid, and contained numerous pus cells and meningococci. A blood culture made the same day (February 8) revealed the same organism. The spinal fluid remained turbid until February 27, though no organisms were found after February 12.

Clinically, the case was regarded as being serious from the onset. Small erythematous spots were noted the second day. The patient was given 60 c.c. doses of antimeningococcic serum intravenously, and 30 c.c. doses intraspinally, as often as four times in twenty-four hours.

February 16, the acute symptoms of meningitis were greatly improved; recovery was expected. Suddenly on this date the patient's temperature rose; his pulse, previously slow, became rapid and very irregular; his lips and fingers were cyanotic. Altogether, his condition became more desperate than it had been at any time. A diagnosis of acute endocarditis was made, and death momentarily expected. A danger card was sent from the ward, which remained effective several weeks. During this time a bilateral convergent strabismus, which began during the first week of illness, became marked; also a partial paralysis of the right arm and leg developed.

March 1, a catheterized specimen of urine was found to contain blood, a large amount of albumin, granular casts, and a few clumps of pus cells. No bacteria were found at this time. Infarction of the kidney and ulcerative pyelonephritis were thought of, but at that time, the patient was too sick for ureteral catheterization. The bladder had to be catheterized frequently to relieve retention. Later the bladder became very irritable and would hold but two ounces of urine without overflow.

When his condition improved sufficiently, the ureters were catheterized, and specimens from both kidneys sent to the laboratory for bacteriologic examination. A direct smear of the sediment revealed many erythrocytes and small clumps of pus cells. One was surprised to find many of the latter containing as many as 5 or 6 Gram-negative diplococci strikingly similar to the meningococci. Cultures were inoculated, upon which appeared numerous soft, clear, refractile colonies, 1 to 3 millimeters in diameter. These colonies emulsified very readily in 0.8 per cent salt solution and the organisms were agglutinated by polyvalent antimeningococcic serum (Rockefeller) in dilutions up to 1:300. Type differentiation, by any of the sera on hand at the time, was unsatisfactory, although known controls at this time were not entirely satisfactory.

The patient gradually recovered the use of his arm and leg, and the strabismus improved. His general condition improved rapidly during his last three weeks in the hospital. He was discharged, upon a surgeon's certificate, July 30, after a stay of 159 days in the hospital. The case is regarded as one of meningococcic septicemia, with localization in the heart and kidneys as well as meninges.

EPIDEMIOLOGY

There are certain outstanding features bearing upon the epidemiology of cerebrospinal fever to which some reference, at least, should be made. Questions have been raised many times, relative to the influence on the spread of the disease, of climatic conditions and of lowered bodily resistance resulting from fatigue and exposure. It has been contended that cold, wet weather is a very responsible factor, and it is true that many more cases of meningitis develop during the winter and spring months than at other times of the year. The evidence against lowered resistance, a term rather loosely employed, is much less convincing. For instance, one seldom sees meningococcic meningitis as a complication or sequela of a long, wasting illness, or following general debility. It attacks, much more commonly, the apparently healthful, robust, young individual. The lowered resistance of the nasopharyngeal mucosæ due to inflammation thereof is much more likely to be a predisposing factor to infection by the meningococcus than is general bodily debility.

Although cerebrospinal fever is classed among the highly contagious diseases, and greatly feared as such, yet the development of consecutive cases does not warrant or confirm such belief. At least, as Frost[3] says, the disease "does not present the epidemiologic characteristics which we are accustomed to associate with a contagious disease. Even in carefully studied epidemics it is the exception rather than the rule to find any direct or even traceable indirect contact between cases." The latter statement applies to our efforts at Camp Cody, which were fruitless, to trace contact between cases, although it was possible in six instances to establish the probability of fairly direct contact between cases and carriers.

A full authoritative discussion of these important questions requires reference to more medical literature than I have access to, at present, and is hardly within the province of this report. It will be sufficient to indicate their application particularly to this camp.

Expressed briefly, climatic conditions at Camp Cody may be summed up in the words "high and dry." The altitude is approximately 4,500 feet, and an hour rain or snowfall during the winter or spring seldom occurs. The winter nights are noticeably cold, though the thermometer seldom registers below zero, F. The sun shines brightly nearly every day. Violent sand storms, sometimes lasting a day, or several days, are very prevalent during the winter and spring

months, and, as stated previously, were undoubtedly the cause of a great deal of nasopharyngitis.

In order to bring out the true relationship of the latter to the incidence of meningitis it should be stated that the sand storms were no more prevalent in February—the month in which the greatest number of cases occurred, than in March, April and May during which time but one case developed. Eighty per cent of the meningococcus carriers which were found, however, were under quarantine by the middle of March.

The element of fatigue was probably of neither greater nor less importance at this camp than at others. Exposure to wet, cold weather was probably very much less here than at other camps in the same latitude and north of it. The daily average mean temperature as furnished by the U. S. Weather Bureau for Deming was 40.6° in January, 53.2° in February, 55.4° in March, and 60.1° in April.

On the whole, the general health at this camp was not far from the average when compared with other camps. With an annual death rate of 12.7 per 1,000 for the six months ending March, 29, 1918, it stood a little lower than midway between the highest, Camp Wheeler, 28.3 and the lowest, Camp Dix, 2.9[1]. Regarding the seasonal occurrence of infectious diseases, the situation may be summarized as follows: an epidemic of measles began early in November, 1917, reaching its high point the week ending December 7. Associated with, and following this epidemic there developed, within the next 45 days many cases of bronchopneumonia. The incidence of primary pneumonias increased rapidly in January, reaching a climax in February. More cases of scarlet fever, mumps and diphtheria occurred during January, February, and March than in any other equal period of time. In fact there was a definite, decided culmination of all the more common infectious diseases during the latter part of January and February, which was also the period of the largest number of cases of cerebrospinal fever. This observation is in keeping with a deduction which Woolley[4] has made, that since "the incidence of meningitis and that of the commoner respiratory diseases are parallel; if, in fact, the appearance of meningitis follows the rise in acute respiratory disease, then one may quite reasonably draw the inference that there is some definite connection between the two." There is reason for believing that the primary infection in all develops in the respiratory tract, and more particularly, the nasopharynx. It is held that meningitis is primarily a nasopharyngitis, the infecting agent gaining access to the meninges either by direct lymphatic extension, or the result of a septicemia, with localization in the membranes of the cord and brain.

There is one element, however, which must be kept in mind. No combination of predisposing causes will give rise to epidemic meningitis without the presence of the meningococcus. Upon a moment's reflection this statement becomes obviously true. Fatigue, exposure to inclement weather, and the existence of a nonspecific nasopharyngitis are highly important, practical factors to be considered in the epidemiology of cerebrospinal fever. Yet, the one necessary element is the meningococcus, and since this organism soon perishes when once it is separated from its natural habitat—the nasopharynx—the problem of its dissemination resolves itself into that of the active meningococcus carrier.

In camp life, the various elements such as close personal association, fatigue and exposure, which unite to pave the way for nasopharyngeal inflammation, can not well be overcome. The other link in the chain, the elimination of carriers, can be broken, and herein lies the rationale of a survey for meningococcus carriers.

It is too much to expect that all carriers in a large cantonment will be found in a single, or, even in repeated surveys. It may be argued that, where only sporadic cases develop, the time, labor and expense involved in such a survey, together with the uncertainty of results, will not justify the taking of such measures. On the other hand, it can not be foretold in the beginning whether cases will develop sporadically or epidemically. Since the aim of a survey is to prevent the latter happening, it should, when circumstances permit, be undertaken very soon after recruits are assembled. This recommendation applies especially in instances where troops are being mobilized from sections of the country in which cerebrospinal fever is endemic. The meningitis epidemics at Camp Funston, and Camp Jackson, have been attributed very largely to the endemity of the disease in Missouri and Kansas, and in South Carolina, respectively. It should be stated here that troops composing the 34th Division which was stationed at Camp Cody, during the winter and spring of 1918, were from the National Guard organizations of Iowa, Minnesota, Nebraska, and South Dakota.

Meningitis is a serious disease by reason of its high fatality, and the disabling sequelæ which are apt to follow it. It has been estimated to be 45 times as prevalent in the army as in civil life, whereas the figure given for measles is 19, and for pneumonia 12[1]. Therefore, it would seem that strenouous measures should be taken against the introduction and spread of this disease, within army camps.

COMMENTARY

Regarding the incidence of the disease in relation to the culturing of this camp for carriers, it is noteworthy that the last case of the series (in point of time) developed February 23, 1918, in a soldier who was a carrier in the Isolation Camp. By this date all companies in which cerebrospinal fever had developed had been cultured and many carriers quarantined in the Isolation Camp under treatment. Whether these two facts stand in anything more than coincidental relationship, it is difficult to say. Only one other case of meningococcic meningitis occurred in the 34th Division before that division left this camp in September. This case developed April 23. Curiously, this patient was admitted to one of the pneumonia wards with a tentative diagnosis of pneumonia. A blood culture made the following day (but after a clinical diagnosis of meningitis had been made) revealed the meningococcus.

During the course of the survey several questions of both practical and scientific interest quite naturally suggested themselves. It would have been interesting to reculture a number of organizations in order to ascertain what proportion of carriers had been missed in the first culture or whether new carriers had appeared. This was done in but one instance, which was occasioned by the development of a case of meningitis in the 126th Machine Gun Battalion thirty-eight days after that organization had been cultured. Nine carriers were found

the first time; two were found the second time, one of whom had been picked up in the first culture. This soldier had been in the Isolation Camp twenty-four days, during which time two positive and three negative cultures were obtained from him. The latter released him from quarantine although the subsequent positive culture would point to the probability of his not being entirely free from meningococci in spite of three negative cultures. No other cases of epidemic meningitis developed in organizations which had been cultured previously.

An investigation regarding the efficacy of the treatment of carriers was proposed, but the stress of work devolving upon the laboratory at this time precluded the undertaking of the purely experimental work involved in this problem. As stated before we relied solely upon the use of a 2 per cent dichloramine-T solution in oil, administered in the form of a nasopharyngeal spray, to artificially hasten the disappearance of meningococci from carriers.

It was reported at Camp Funston that this spray, induced hyperemia about the orifice of the eustachian tube followed by the development of cases of otitis media. At Camp Cody no untoward results were observed from this source.

SUMMARY AND CONCLUSIONS

1. It is a safe prediction that cases of epidemic meningitis will develop wherever large numbers of recruits are assembled and live together for any considerable length of time, in close quarters. The intimate personal associations, unavoidable in camp life greatly favor the dissemination of the disease; hence, the potentiality of a serious widespread epidemic.

2. The dissemination of cerebrospinal fever depends ultimately upon the presence of meningococcus carriers, although the existence of a nonspecific nasopharyngitis is undoubtedly a predisposing factor in the development of the individual case.

3. The period of greatest incidence of meningitis may be expected when the more common respiratory infections are at their height, due to the fact that in all of them, nasopharyngitis is a primary and predisposing factor. The greatest number of cases of the latter develop when living conditions are at their worst.

4. In military camps, where large numbers of troops are mobilized from sections of the country in which meningitis is endemic, the possibility of the disease becoming epidemic is greatly increased, by reason of the greater proportion of meningococcus carriers. A determined effort should be made, in such instances, to eliminate the carriers as quickly and thoroughly as possible. A general bacteriologic survey is the only logical means to such an end, and although its accomplishment on the large scale necessary in the average camp is fraught with many practical difficulties, it should be undertaken.

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[3]Frost: Epidemic Cerebrospinal Meningitis, Public Health Reports, U. S. P. H. S., 1913, No. 69.
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THE ROLE OF TUBERCULOSIS IN DEMENTIA PRECOX*

(Second Report)

By H. I. Gosline, M.D., Worcester, Mass.

THE following report is intended to supplement the Preliminary Study† of the same title and is the extended account of the seventeen cases mentioned there, in which the connection between the mental and the physical disease was so close that certain writers have considered the one as due to the other.

The history of the case which may be considered to serve as a type for the other seventeen cases and which will have occurred in the experience of every psychiatrist, is as follows:[1] A girl of 27, of tuberculous build and who has shown signs of latent tuberculosis, remains depressed and introspective following some disappointments. There appear difficulties of attention, cerebral torpor, absent-minded periods, then transitory ideas of persecution and feelings of hatred against her parents.

After several weeks there follows a melancholic state with stereotyped writing.

Soon after there suddenly appear catatonic manifestations: prolonged immobility, negativism, cerea flexibilitas, cataleptoid attitudes, stereotyped movements, suggestibility. A slight remission was observed during the next few months but the automatic manner and the stereotypies were maintained. The mental condition is slightly affected in spite of appearances; no confusion, no disorientation, conservation of the feelings of hatred against her parents and of the sense of shame.

Admitted following the remission. Fixed positions and catatonic phenomena resumed. Progressive cachexia. From time to time a slight febrile reaction is noted, with headache and epistaxis associated with a tuberculous infection which is developing at the apices of both lungs.

The autopsy showed that we were dealing with a case of fibrocavernous tuberculosis. A study of the organs and of the glands of internal secretion revealed nothing abnormal. In the nervous system was seen a sclerous meningitis with small hemorrhages, in various stages of evolution, and distention of the arachnoid spaces with edema. The examination of the cortex, etc.

The study of the clinical symptoms and the anatomic findings leads the authors to decide upon the diagnosis of melancholia with stupor of dementia precox, in spite of the existence of the catatonic syndrome. They are of the opinion that this agrees with the conception of Regis and certain other authors who think that intermediary forms exist between certain forms of chronic mental confusion of toxic-infectious origin and dementia precox.

There is opportunity to mark out the domain of this psychosis, with the aid of carefully compiled clinico-anatomic data. The syndrome of Kraepelin seems to be realized by two types of psychosis: the one which is really worthy

*From the Laboratory of the Worcester State Hospital, Worcester, Mass.

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of the name dementia precox, is a constitutional psychosis, following puberty independently of toxic or infectious causes.

The other type would be a form of toxic-infectious psychosis, often of tuberculous origin, which would take the form of dementia precox but would not always lead to dementia and would be curable in the cases in which the meningeal and encephalitic lesions were not pronounced and were halted in their course. The future will tell whether such a division, interesting from the point of view of prognosis, is justified by the discovery of symptoms and of lesions characterizing the two varieties of the hebephrenocatatonic syndrome.

Following the plan in the previous paper, the tabular view form of presentation is adopted. The cases are as follows:*

As was pointed out in the first paper, we are dealing with a special, selected group of cases. These cases were selected because they were undoubted cases of dementia precox; all of them could be placed in the catatonic group or the hebephrenocatatonic group, as some writers would have it. With the whole material now before us there will be some doubt expressed as to the grouping. Were they really cases of dementia precox? In the discussion which followed the reading of the French paper it was claimed that the case was not one of dementia precox because the affectivity was preserved, "the patient showed animosity and affection for certain individuals till the end." This was considered prima facie evidence against dementia precox. The question might be raised as to whether even this retention of the affectivity would have had weight before death in making the diagnosis against dementia precox in face of the negativism, cerea, and stereotyped movements which the patient displayed.

In our group of seventeen cases there are some even more clean-cut cases of dementia precox, in which the question might be raised with all the material now before us. A review of the cases shows three main groups: the agitated depressed, the apathetic stupor, the hysteriform. There is a poorly defined mixed group in which agitation and apathy combine or alternate. To the first group belong Cases III-6, III-24, XVI-23, XVII-43, 14-7. Related but without the depression are Cases IV-16, IV-18, V-3. To the second group belong Cases III-14, 1916.25. To the third group belong Cases III-31 (agitated), VII-41 (agitated depression). To the mixed group belong Cases XII-28, (agitated stupor), XIII-17 (agitated apathy). Two cases (III-43, VIII-3) were first agitated and later apathetic, and one case (IV-8) was first stupid and later active. If we were to place the French type case in one of these groups, we would be safe in considering it one of hysteria, major form, though the cardinal signs are absent. The stereotypies and attitudes might equally well be hysterical or catatonic as far as the presentation of the case is concerned.

The terms used to describe these groups, while more or less generally discarded like melancholia attonita, still may serve to convey the total effect of a case upon the observer and as so used may still have some value. Using them in this way we have three main groups and these are the groups so frequently associated with infections other than tuberculosis. If we consider our cases of dementia precox in this way, may we not arrive at a differentiation of the two

*Signs have the same meaning as in previous paper. Numbers after symptoms or signs refer to number of days of month each was present.

Case III-6

MENTAL

1896—Onset with depression and agitation. Auditory hallucinations, delusions of persecution and of poisoning. Tube fed. Assumed fixed standing positions. Spent night on knees, praying in the coldest weather. Fear affect.

1897, March—Negativistic, resistive, tube fed. April—Delusions of poisoning. Cries but stops at once. Stares, practically mute. May—Aggressive. June—Eats voluntarily but secretly. Says his "stomach is broken." Stands like a statue with head bent and resists being moved. August—Explains his financial troubles. October—Tube feeding again for 10 days.

CONDUCT CHART	
Year, 1897	
Month, 10	
NOISY	×
TUBE FED	±
SLEEP POOR	±
APPETITE POOR	×
ILL	×
UNTIDY	×

PHYSICAL

Anemic, bad capillary circulation, obstinate constipation, foul breath, insomnia.

1897, April—Spits. Five feet, ten inches tall, weighs 180 pounds. Rigid muscles.

October—Continued pyrexia. Rales both lungs. Prolonged expiration upper lobes.

November—Emaciation, pain in both chests low. Fetor and when on left side, cough with foul expectoration. Exit.

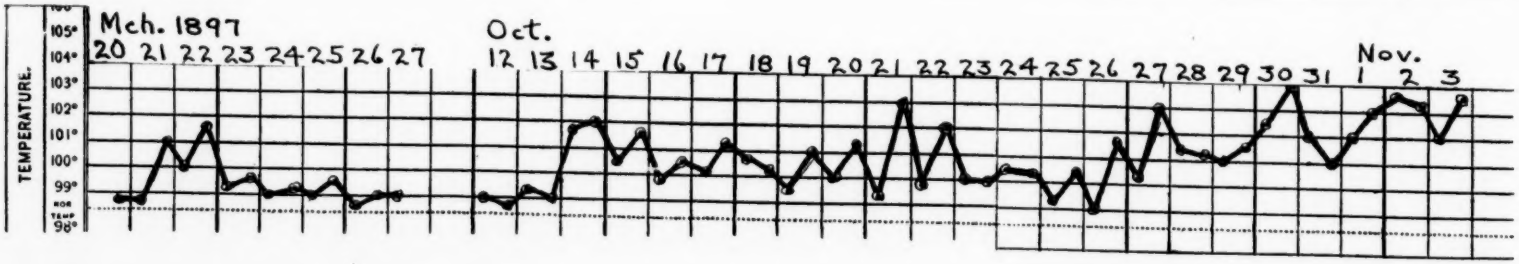
SUMMARY

Patient, age 29 or 46 (error in dates), has physical signs often found in tuberculosis and develops an acute catatonic condition which continues till death two years later. Two months before death active clinical tuberculosis develops.

Autopsy reveals adhesions posteriorly over right lung and at apex of left. Right lung consolidated, most marked at anterior, inferior, and interior portions. Firm, light, reddish gray, with rough, uneven feel at apex where it is nodular. Middle lobe shows abscess. Wt. 1227 gm.

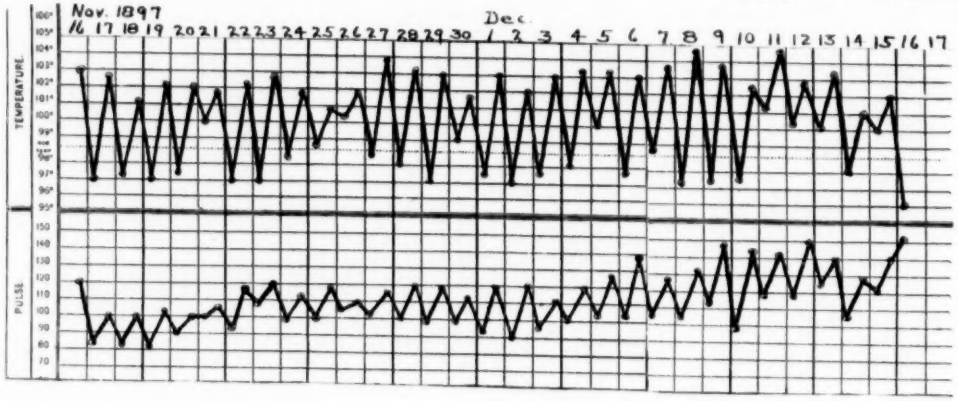
Left upper lobe seat of small hard nodules of slate gray color, most at apex. Consolidation posterior border. Lower lobe shows gangrenous cavity and is consolidated, except the anterior border. Color pinkish gray with opaque gray, marble-like areas. Wt. 1048 gm.

Over pons, beneath basilar artery is an extravasation into pia, jelly-like, resembling tapioca



Case III-14

MENTAL	PHYSICAL	SUMMARY
From the age of 10 different from other boys. 1892—Change of character. 1895—Everyone dominates him, no self-control, can not think. Dull, morose, reserved, "temper." Facial mannerism. 1896—Careless, stupid, silly, cerea. 1897—Sits in one position for long periods. Tube fed, irrelevant, incoherent, orientation for time poor, remote memory poor, no insight. Apathetic stupor.	Masturbated since 6 years of age. 1895—Speech hesitant. 1896—In bed. 1897—Loss of appetite. Emaciation. November—Percussion flat at inferior angle of right scapula, respiratory sounds absent. Same left side and friction rub over left lower lobe anteriorly. Hyperresonance elsewhere. December—Exit.	Gradual change in an abnormal individual. Active physical signs noted one year after active mental symptoms begin. Come to examiner's attention one month before death. Autopsy—Intestines distended. Adhesions through left chest except outer surface lower lobe. Cavity at apex. Right lung 1180 gm. Consolidation of upper lobe except apex and lower lobe except inferior parts and edges; partial consolidation of middle lobe. Many caseated cavities in upper lobe, tubercles in middle and lower lobes. Left lung 1240 gm. Lower part of lower lobe crepitant. Upper lobe solid with many cavities. Lower lobe many tubercles. Two accessory spleens.

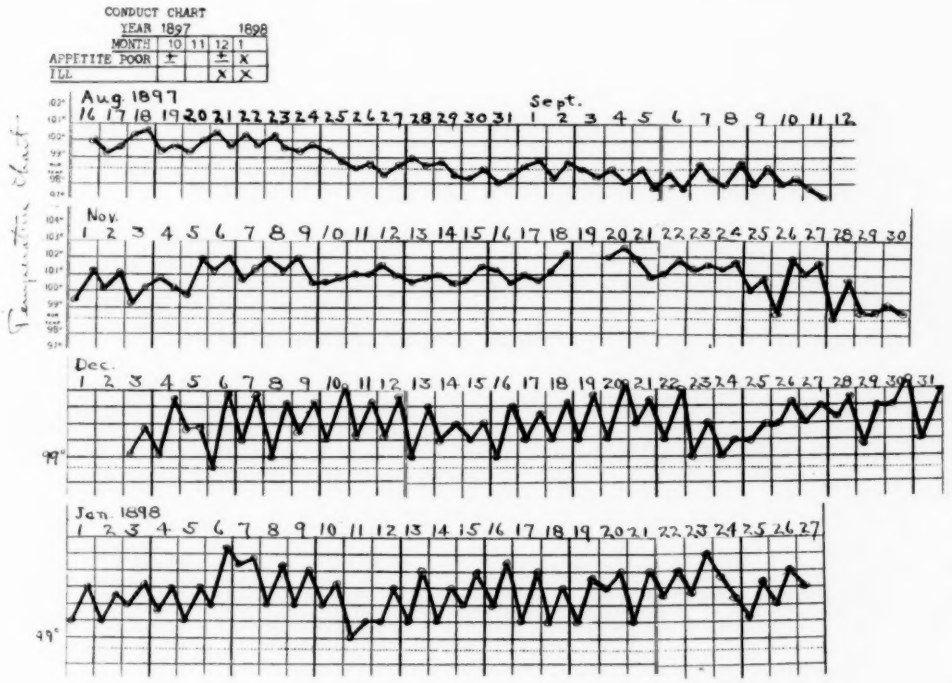


CONDUCT CHART
YEAR 1897

	MONTH	10	11	12
UNTIDY		X	±	
APPETITE POOR		±	±	±
ILL		X	X	X

CASE III-24

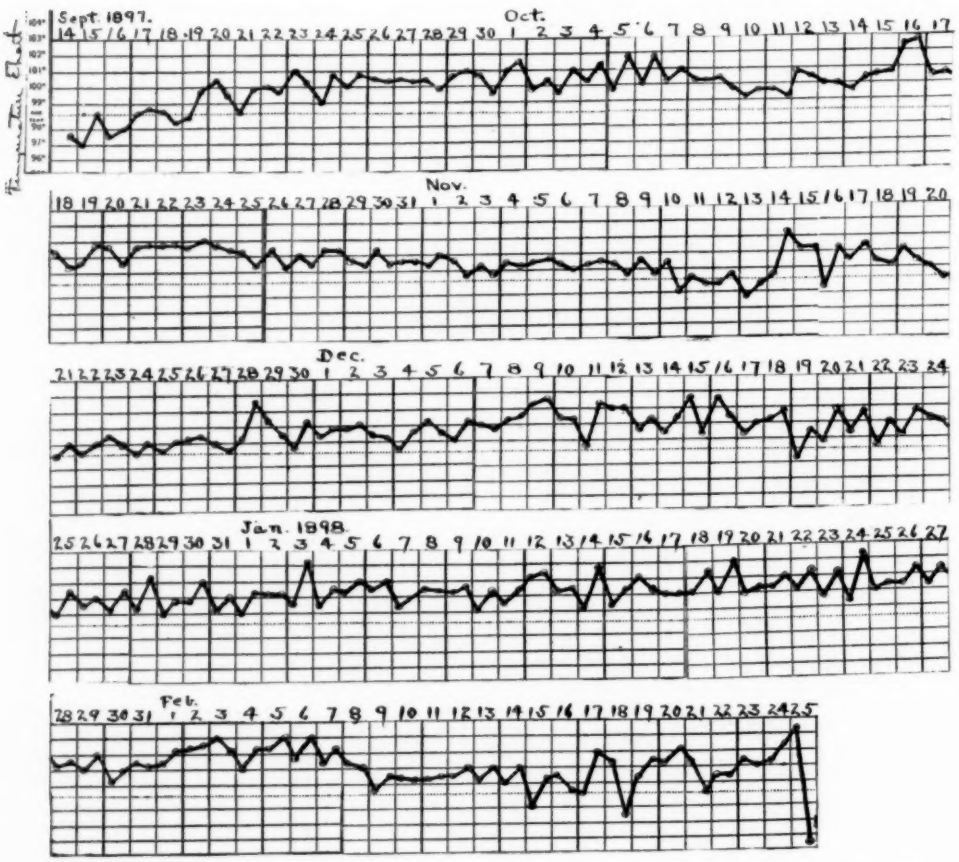
MENTAL	PHYSICAL	SUMMARY
1897—Depressed, somewhat excited. Auditory and visual hallucinations. Hesitates and repeats answers. Points to heaven. Throws head to right forcibly. Prays, grimaces, walks about house, will not address wife. Thinks Catholics will shoot him. Disoriented for time. "Medicine is pumped up from sink." Mute at times. Sexual delusions. Confused, incoherent. Stereotyped movements and attitudes. Destructive at times. October—Shows some insight. November—mannerisms. December—Does not know why he is mute.	1897—Health failing gradually. Insomnia. August—Pain in chest, white foaming sputum. September—Sudamina forehead, temples and chin. Sebaceous scales. November—Says he "spits and bleeds and aches in his chest." December—Flat right apex and subclavicular region. Percussion causes cough. Dullness posteriorly throughout, more at apex and interscapular border. Bronchial breathing apex and scapular border. Rales in second space. 1898, January—Cough and bloody expectoration on passing tube for feeding. Other hemorrhages later. Catheterized. Exit.	Failure in physical health and development of tuberculosis runs parallel with the mental symptoms. Total duration less than two years. Autopsy—Bladder to umbilicus. Intestines distended. Mesenteric glands enlarged and nodular. Right lung, wt. 1415 gm. Cavity size of an orange at apex, others throughout lung. Upper and middle lobes consolidated. Numerous tubercles about bronchi, lower lobe. Left lung, wt. 673 gm. Adherent throughout. Upper lobe consolidated with numerous caseated cavities. Similar areas at anterior margin of lower lobe. Accessory spleen.



CASE III-31

CONDUCT CHART

YEAR	1897			1898	
MONTH	10	11	12	1	2
EXCITED	±				
NOISY	±	±	X	X	±
RESTLESS		X	X	X	X
UNTIDY	X	X	X	X	X
TUBE FED	X	±	X	X	X
SLEEP POOR	±	±	±	±	X
APPETITE POOR	X	X	X	X	X
ILL	X	X	X	X	X



(See Table, page 403)

CASE III-31

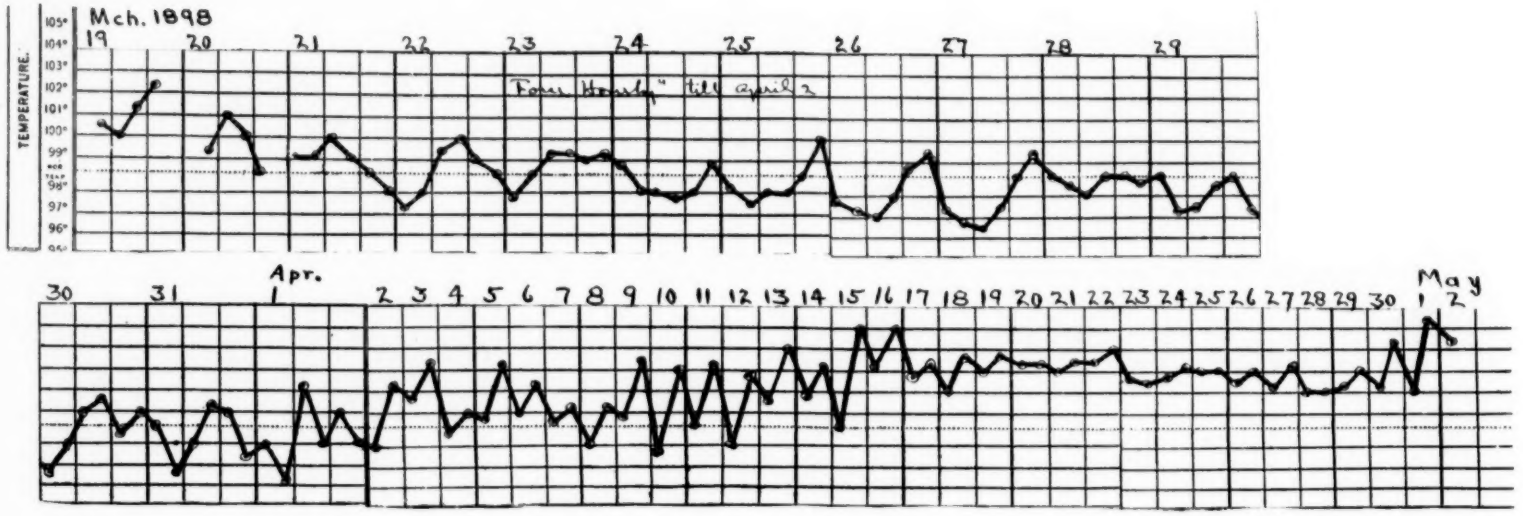
MENTAL	PHYSICAL	SUMMARY
1897—Saw caterpillars and animals on the wall at times, refused food, talked incoherently and loudly, mumbled and stared. Auditory hallucinations, violent, threatening, feared she would be burned up. Said people hit her and wanted the bumps examined. Felt exalted in her religion. Thought her limbs were gone and that it was done by electricity. Disoriented. At first said her trouble was in her brain. Answered promptly but irrelevantly at times. Restless and once held a fixed position. September—Thinks she is not at home when she is. Thinks clothes are on fire. Insolent, lewd, profane, tries to leave house unclad, screams. Sept. 21—Grasps at objects near, people, bedclothes, etc. Staring, forehead wrinkled. Says, "I don't know how, where." Affect of fear. Mutters low and unintelligibly. Moves arms about in purposeless manner. Becomes more stupid, drools, untidy, tube fed, holds food in mouth till it runs out. Disoriented, smiles in silly manner. Sang at night, smiled once at joke, moves lips. Questioned, laughs quietly, then cries without tears. Sept. 30—Noisy when moved. October—Catatonic, irrelevant. November—Delusion of negation, untidy, says she is insane. 1898, January — Oriented and calls nurses by name. "At times does not see people well and does not know them." Thinks she lost a foot and wishes physician would see. February—Threatens suicide.	Father and uncle nervous. Maternal uncle "foolish" after scarlet fever. Two paternal aunts and brother died of tuberculosis. Paternal uncle and brother died of cancer. Three children nervous, two miscarriages. Semi-invalid after birth of first child at 26 or 28. Would wake up choking last two years. 1896—Would become rigid but had no convulsions, called "spasm." 1897—"Spasms" sometimes preceded by a scream, lasted 1 to 2 minutes. Insomnia, poor nutrition, poor muscular tone, face flushed, extremities cold and anemic, feels exhausted. Urine shows s. p. t. albumin. Sept. 21—Skin of mouth and forehead scaly. Sept. 30—Pharynx congested. October—Diarrhea, tongue coated, scales at corners of mouth. November—Decubiti, emaciation, cough with expectoration. December—Rales anteriorly and dullness posteriorly on right. Sputum negative. 1898—February—Arms, legs, and feet swollen. Death.	Patient a semi-invalid for some time and with a strong hereditary taint, goes into a confused, muttering, delirious state with catatonic features. The physical condition rapidly becomes poor and ends with signs of tuberculosis. Autopsy—Decubiti. Petechiæ over abdomen and chest. Extensive adhesions right, few over left lung. Right lung indurated with large nodes made up of "slightly confluent tubercles of caseous decay." A few cavities appear at the apex. Left lung shows nodules in posterior and middl parts of upper lobe and in lower part of lower lobe. Many confluent groups of tubercles appear on section.

(See Chart, page 402)

CASE III-43

CONDUCT CHART
YEAR 1898

MONTH	3	4
UNTIDY		±
ILL	±	×



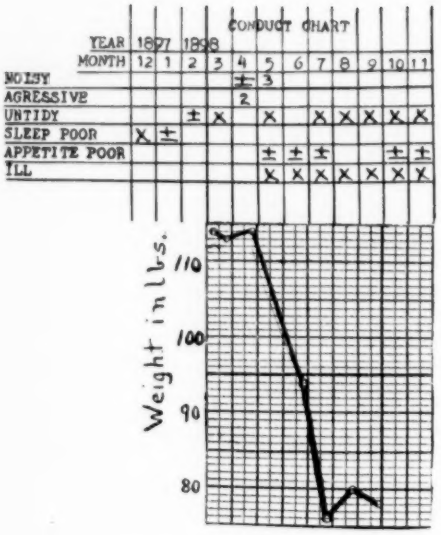
(See Table, page 405)

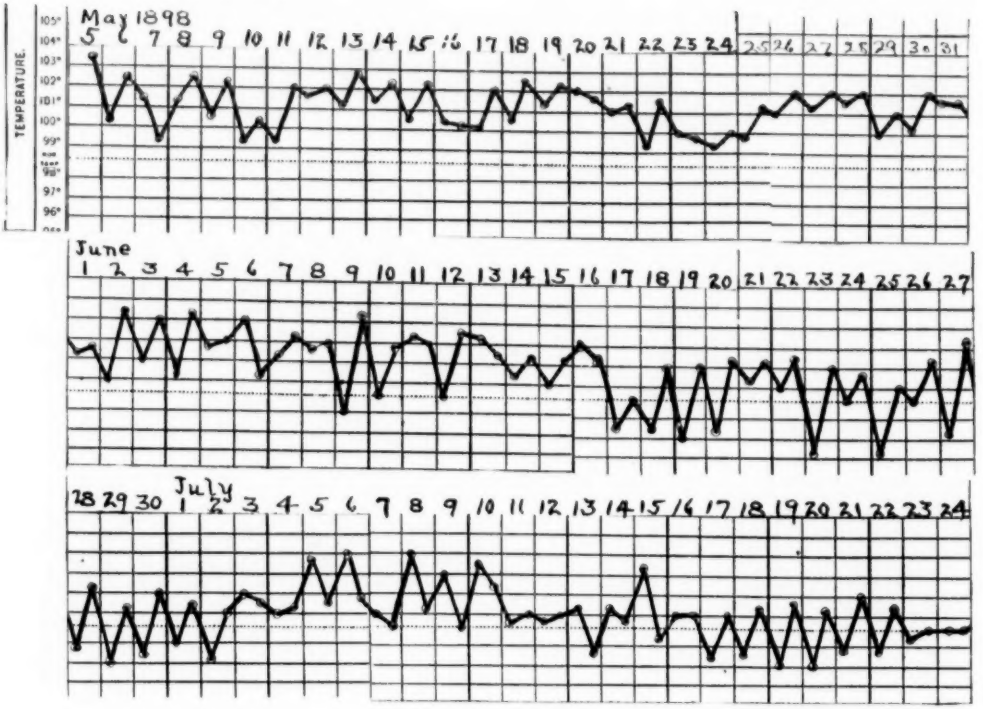
CASE III-43

MENTAL	PHYSICAL	SUMMARY
Always reticent. Six months before active onset said "peculiar things" and had buzzing in the ears. Two weeks ago affect of fear. Delusions of persecution, suicidal attempt, violent, dangerous. 1896, January—Hallucinated, restless, dazed, confused, incoherent, suspicious. February—Improves. June—Dull and apathetic. July—Irritable. October—Threatening, masturbates, sits in one position all day. 1897, May—Dull, unoccupied. June—Mannerisms. September—Talks to self, untidy. 1898, January—Indifferent. April—Mute, will not open eyes.	First lost weight. 1896, July—Began to gain weight. 1898—March—Weak, mitral murmur, legs swollen. Bubbling rales left lung, friction rub, dullness. Cough, temperature, t. b. abundant. April—Knees have gradually flexed. Right hand paralyzed in flexion. Epistaxis. May—Death in stupor.	Gradual onset with dazed, confused attitude, followed by improvement and relapse. Initial loss of weight, then a gain, and finally dementia precox, contractures and positive sputum. Autopsy—Right lung shows small nodules. Left lung adherent throughout. Contains hard nodules, infiltrated foci, and some caseated and abscess areas. Nodules in left kidney and in liver.

(See Chart, page 404)

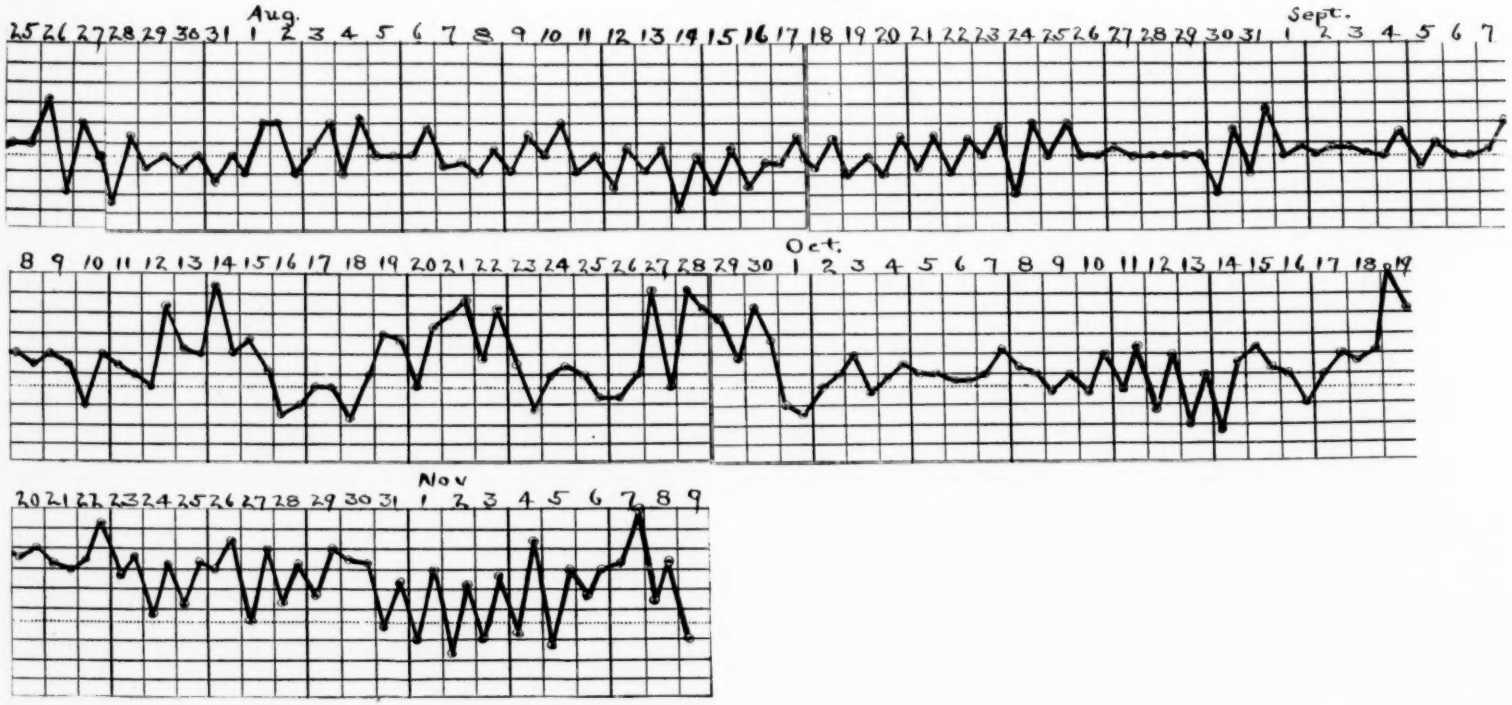
CASE IV-8





(See Table, page 408)

CASE IV-8—Cont'd



(See Table, page 408)

CASE IV-8

MENTAL	PHYSICAL	SUMMARY
Over a year ago thought meat bad for the head. 1897, January—Washes oftener than usual. Saw a cat on two legs like a man and heard devils cursing him and saying they would get hold of him. March—Would sleep in chair at dinner, stupid and staggered on rising. Delusions that enemies were trying to poison him. Confused, replies uncertain, memory defective. "Puzzled in mind, kind of dreaming." Sexual ideas, irrelevant. April—Muscular rigidity. May—Dribbles saliva, refuses food, mute, stereotyped movements. Insight, none. July—Aggressive. September—Untidy. 1898, May—Thinks he has died and is different. The world has come to an end. Irrelevant, incoherent. A young woman comes to him in spirit.	Has masturbated since the age of 10. 1897, January — Insomnia. April—Acne arms and back. Knee jerks exaggerated, arms rigid, tremor of hands and tongue. December—Mitral murmur. 1898, May—(?) pneumonia right upper lobe and nephritis. Later sweats and tuberculous temperature. August—Sputum positive. October—Decubiti, weak. November—Exit.	Onset with active mental symptoms which soon lead to a confused, stuporous existence. Signs of active pulmonary disease noted first over a year after mental trouble began. Autopsy—One liter of fluid in chest. Right lung adherent throughout. Gray nodules present and confluent areas with caseous lumps. Left lung, adherent upper lobe, lobe nodular. In lower part are many cavities with slimy pus and gray gelatinous nodules in hardened tissue.

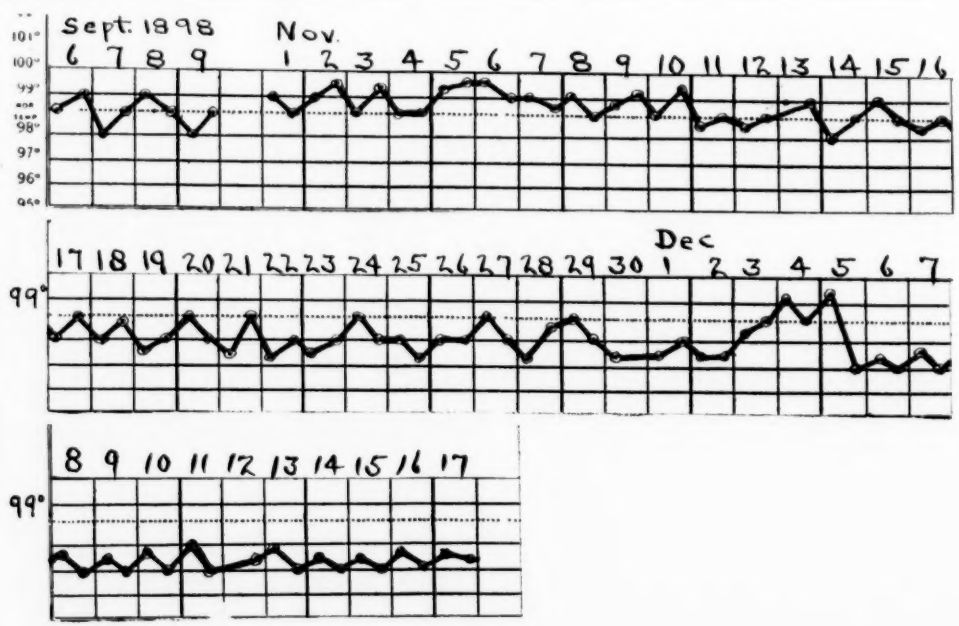
(See Chart, pages 406 and 407.)

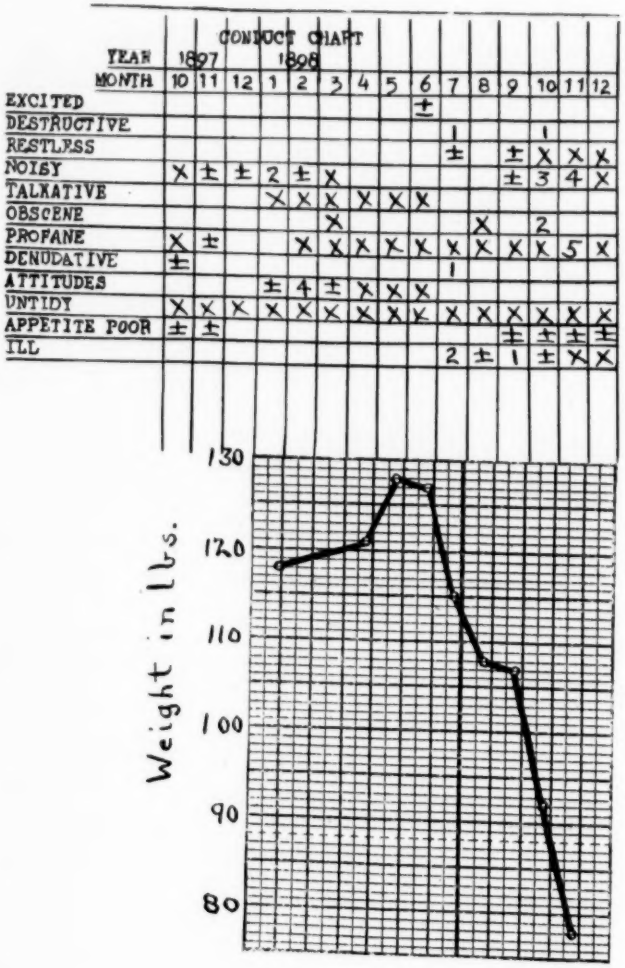
CASE IV-16

MENTAL	PHYSICAL	SUMMARY
1898, August—Hysterical laughing and crying. Suspicious. September—Excited at times. "Policemen are hunting her on the street." At times violent, excited and destructive, then confused, dull and untidy. On admission was irrelevant, incoherent. Had a "wild stare," moans, holds lips firmly together, negativistic, pulls her hair out, removes her clothing, is resistive, restless, tube fed. October—Stiffens her body when fed. November — Screams. (?) thinks some one is in her room.	One sister said to be similarly affected. September—hyperhidrosis. Later "cheeks more sunken." October—Epistaxis. Pregnant. November—Child born. Knee jerks exaggerated. December—Decubiti, weak, emaciated. Exit.	A mixed active and dull confused state with catatonic symptoms and terminal fear affect. Physical picture clouded by pregnancy but final signs. Autopsy—Right lung firmly adherent anteriorly and posteriorly. Nodules at apex and in lower lobe. Left lung the seat of nodules of egg size to pea size, firm or slightly soft. Bronchial glands enlarged.

CONDUCT CHART
YEAR 1898

MONTH	9	10	11	12
EXCITED	X	X		X
RESTLESS	X	X		X
NOISY	±			±
IRRITABLE	Z	X		
AGGRESSIVE	Z			
RESISTIVE				X
DENUDATIVE	X	X		
UNTIDY	X	X	X	X
SLEEP POOR	X	±	X	X
APPETITE POOR	X	X	X	X
ILL		±	X	X

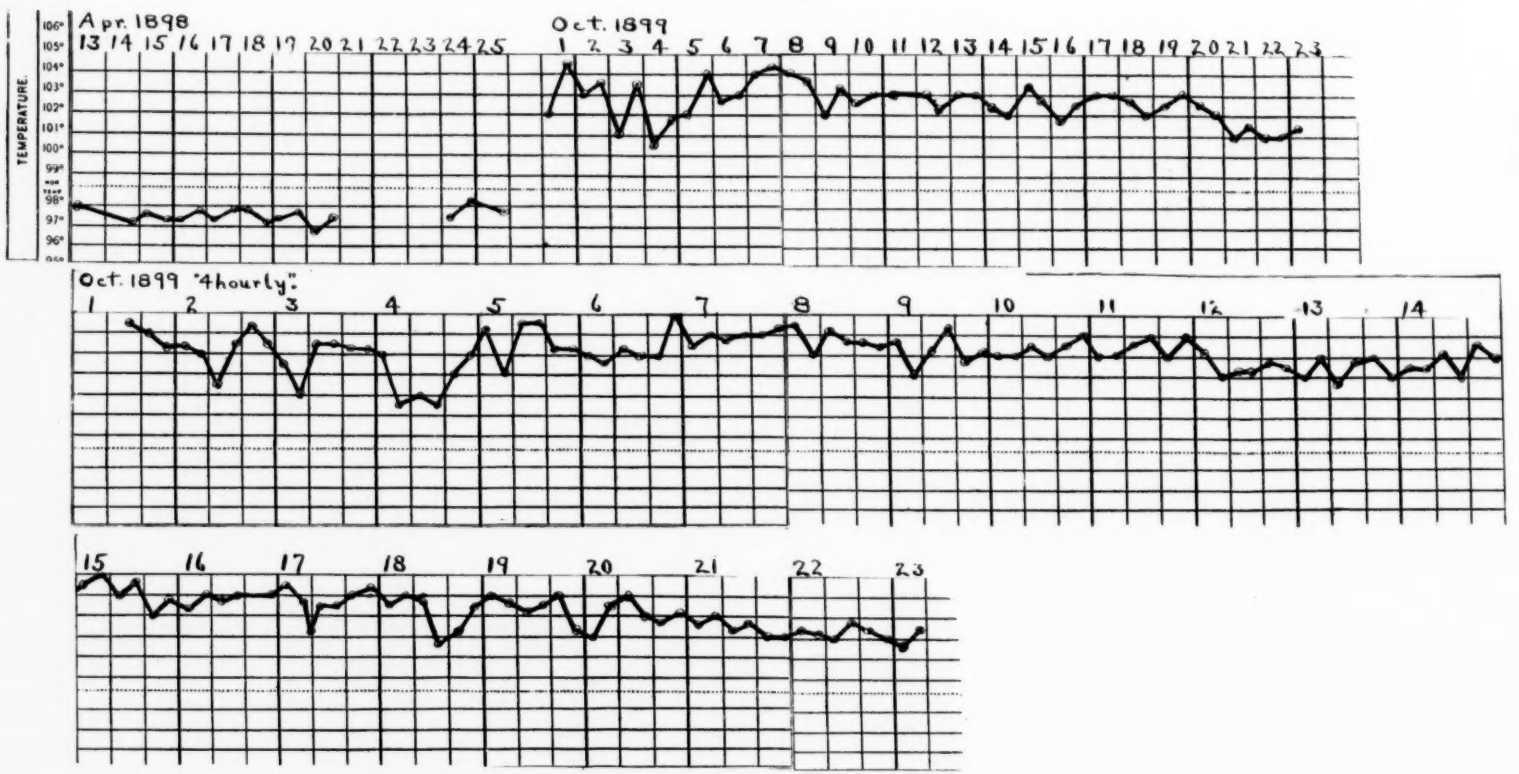




Case IV-18

MENTAL	PHYSICAL	SUMMARY
1897, January—Christ and the Virgin appeared to him. February — Peculiar actions, spitting, answering employer or not as he liked, walked around a building six times, etc. March—Sexual ideas, irrelevant. Spits and talks over his right shoulder "because he tells the truth to the right." God wants him to go through these "performances." Stereotyped positions, movements and expressions, cerea, disoriented for time. Answers after long pause. Mutters a word salad. Says words "that surprise himself," neologisms (pidginess). May-June—Rubs head with handkerchief, "a snail is in his head and in his finger." October—Becomes untidy. 1898, January—Cerea, stereotypies, gesticulates, attitudinizes. February—Silly, uncontrolled laughter, incoherent, irrelevant, sometimes mute, noisy, violent.	Probably illegitimate child, masturbates occasionally. 1897, March — Pain sense impaired, skin can be pierced without patient flinching. 1898, July-August — Feet swollen, mitral murmur. December — Only recorded temperature 97.6°. Left apex flat, loss of weight, cachexia, bolts his food. Later dry rales. Exit.	Sudden onset at 22 years with catatonic symptoms which soon lead to complete disorder of conduct and thought connections. Early impairment of the pain sense and late evidence of tuberculosis. Autopsy — Decubiti. Right lung adherent at apex, left pleura obliterated throughout. Left upper lobe indurated, some hemorrhage present and some small yellow nodules.

CASE V-3



(See Table and Charts, page 412.)

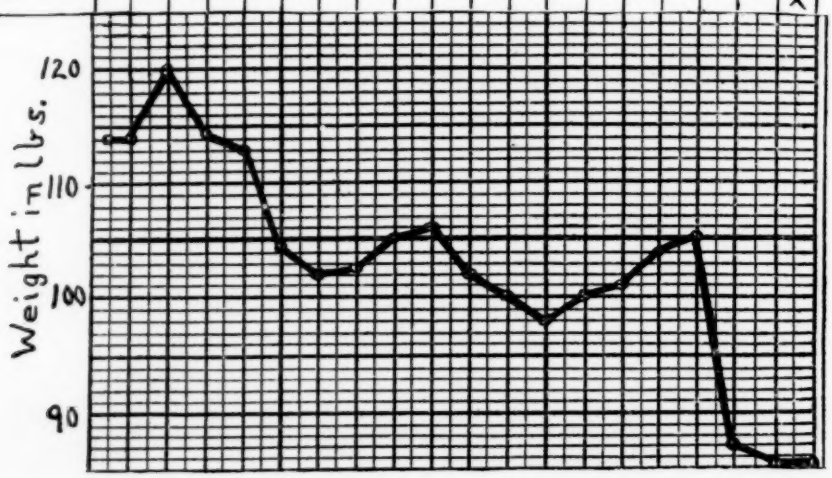
CASE V-3

MENTAL	PHYSICAL	SUMMARY
1897, May—Talked and worried about the future. June—Silly laughter, claims that she sees a man who wants to talk to her. Later "spells of crying." Took a vacation during which she attempted suicide twice. September—Irrelevant, "as bad as ever." 1898, February—Since September alternate improvement and relapse. Now thinks she can communicate with people on the street. Will talk and then stop as if listening. Said her father paid the doctors to keep her in the condition she was in. "They would do better to get her a young man." Violent, untidy, talked love, had to be dressed. April—Impulsive, decorates, poses, auditory hallucinations, restless, erotic, will not help herself, oriented. May—Resistive. July—Irrelevant, incoherent, silly. August—Shakes body, obscene, aggressive. September—Untidy, helpless and aggressive. October—Masturbates. November—Fixed attitudes, horror of bathing. Condition similar for the next year.	Maternal aunt and mother insane. 1897, May—Loses flesh. 1898, April — Papular eruption on face, forehead, back, chest and arms (acne vulgaris). Comedones on cheeks. 1899, October — Pneumonia. Later, sputum positive. Exit.	Mental symptoms come on gradually at 23 years. There is a continuously active sexual trend with deterioration in one year and death in less than two years. At the beginning there is a loss of weight and after admission to the hospital a continuous loss but no determined diagnosis till the last month of life. Autopsy—50 c.c. blood-stained fluid in each chest. Old, firm adhesions both lungs, left upper lobe anteriorly and laterally and posteriorly at the apex. Right lung, lower part of upper lobe consolidated, middle part shows numerous clusters of nodules, lower lobes less numerous nodules. Left lung, numerous cavities upper lobe, one 4x6 cm., lower lobe studded with small nodules.

(See Chart, page 411.)

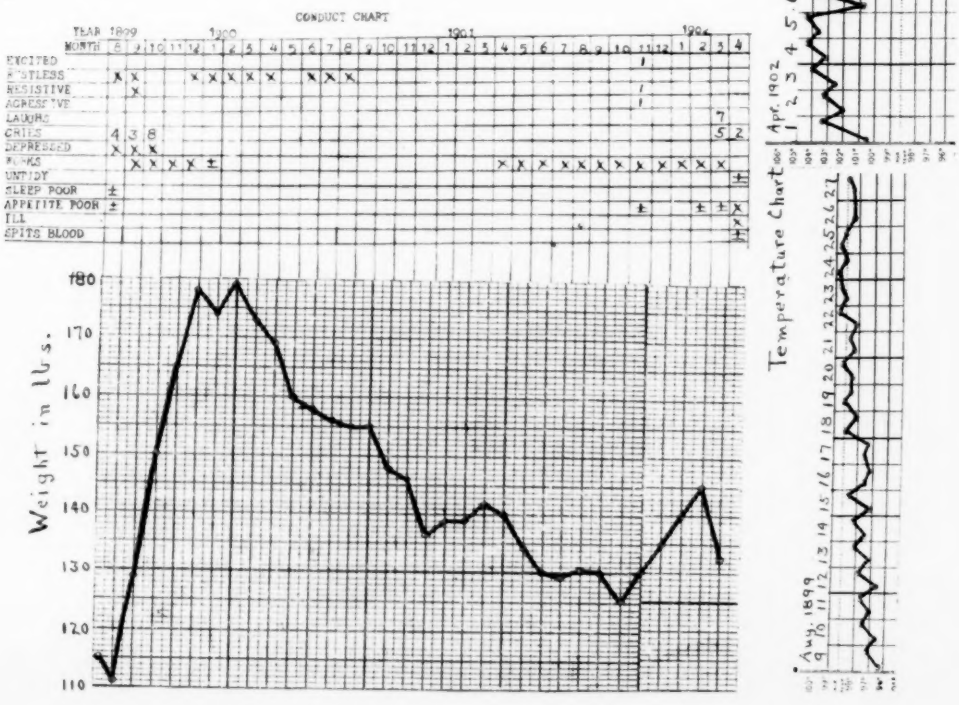
CONDUCT CHART

YEAR	1898									1899								
MONTH	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10
EXCITED		1				X				X	X	X	1	X		X	X	X	5
RESTLESS	X	X	±			X		X			X			X	X	X	X	X	X
NOISY	X	X	±							X						3			
IRRITABLE						1	X										3		
AGGRESSIVE					1	1				3	2					2		1	
ABUSIVE						1													
RESISTIVE									6	X	X	X	X	X	X		X	X	X
LAUGHS																	2		
DENUDATIVE						X		X	X	X	X		X		X	X			
MASTURBATES							X	X					X	X	X		X	X	1
UNTIDY		4				X	X	X	X	X	X	X	X	X	X	X	±	X	X
SLEEP POOR	±	X	2	±	±		4			±	±	±		±		±			X
APPETITE POOR	±			±						±									X
ILL																			X



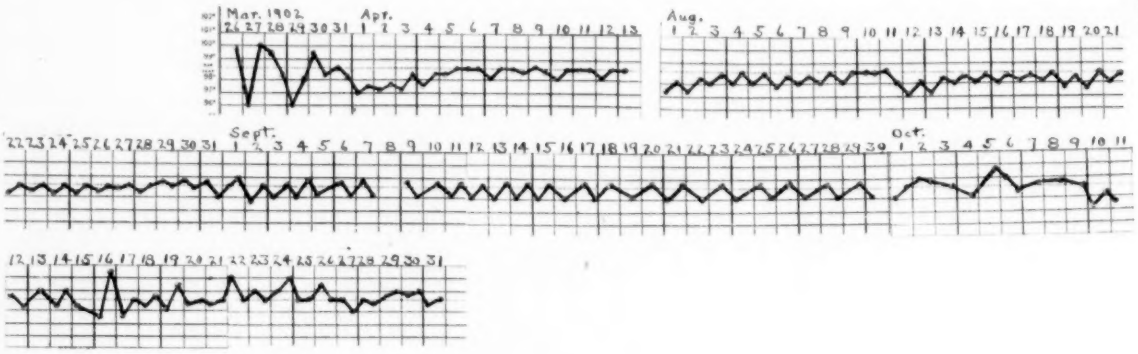
CASE VII-41

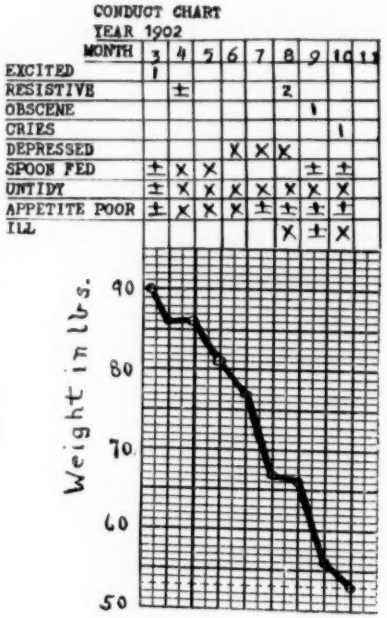
MENTAL	PHYSICAL	SUMMARY
Two or three years ago had nervous prostration. 1898, November—Had delusions of poisoning against nurse at last confinement. Suspicious of doctor, husband, and mother drugging medicine. Auditory hallucinations. 1899, January—"Husband unfaithful with patient's mother." Cries, excited, abusive, aggressive, then remorseful. Spring—Knows when spells are coming, "a cloud comes over her brain." July—Applies for divorce (has cause). August—Stays out late nights with baby. Memory poor, orientation good, insight partial, "worse since coming to hospital." September—"Hears four different kinds of noises in her head at once," negativistic. October—Cries, "abused by everybody," "imagines she sees false objects," "has a whirling in her head," "hears voices," "queer feeling in her head affects her heart," "a heavy feeling in her stomach." 1900, May—"I imagine that I am living and again that I am not," "I can not explain it for my mind goes from me and I am not here." December—Violent, aggressive, appropriates belongings of others, resistive, tries to escape. 1901, August—Auditory hallucinations; carries head high and hair in a peculiar fashion.	Paternal aunt insane, father a suicide, brother peculiar. Menses at eleven, regular. At 14 came every 2 to 3 weeks and lasted 4 to 5 days. Appetite poor. Married at 19, because pregnant. 1898, November—Headaches. 1899, January—Weak. September—On getting up is dizzy and head goes round and round. Lies down much, "weak and lifeless." December—"Too weak to do anything." 1902, March—Never heard to cough, appetite poor. April—Hemorrhage from lungs, "cheesy particles," no bacilli. Cough, rales. Stupor. Exit.	Active onset at 24 in a person somewhat handicapped with heredity at the start. Condition progresses over a period of three years or less, with insight at first but lost later. Obscure physical signs persist, almost from the start but definite signs appear only in the last month of life. Autopsy—Right pleural cavity obliterated, upper part of left upper lobe adherent. Right lung shows a large number of hard nodules, apex on solid mass of tubercles, lung cuts like liver. Left lung, large tubercles and pneumonic gray areas, two cavities at apex and several elsewhere. Pus points over bronchi. Bronchial glands enlarged. (?) Tubercles of pia.



Case VIII-3

MENTAL	PHYSICAL	SUMMARY
Seclusive and religious. 1901, March—Constantly talking religion, irritable, wanders on street, refused food, untidy, drools, spits, mute for past six months. Injures self by bumping head. 1902, March—Holds positions, fingers flexed in hands, negativistic, tube fed, inactive, irresponsive. April—Motionless, resistive. June—When touched jerks sharply away. October—Profane, talks after long period of muteness, resistance in eyelids later. Stereotyped expressions. Thinks some one is under her bed. Speaks of dying. Mute at times, resistive, negativistic, disoriented, confused. Says she spits up brown stuff that looks like chicken but it goes down again. "I used to sleep and never wake up, of course I didn't die." Memory poor.	Brother insane (?). 1901, March—Insomnia, loss of weight. 1902, March—Offensive nasal and vaginal discharge. Edema of feet and upper lids. Reflexes exaggerated. Appetite poor. July—Bed for weakness. October—Limbs cold, temperature begins. No cough. Asks for brandy for diarrhea. November—Complains of being smothered. Exit.	Active mental and physical symptoms begin at 44. Both persist unabated till the end about a year later. Temperature said to begin two months before death. Autopsy—Cause of death: Pulmonary tuberculosis (protocol missing).





CASE XII-28

MENTAL	PHYSICAL	SUMMARY
1906, September—Stupor of 6 to 8 hours' duration. October—"Going to be cut," wishes he were dead. Can not get well, has no life, is all gone. Careless, unsociable. 1907, July—Mute few days, screamed, refused food, "everybody is eating too much," "people called him a freak." Says he has not been well and that the night before admission was a blank to him. Answers slowly and stupidly. Staring for three weeks, solitary. On admission was resistive, suicidal, noisy and mute.	1906, September — Violent headaches, anemia. 1907, July—Has lost weight past year. Insomnia last three weeks. Systolic murmur at apex, over precordia and in axilla. P.M. rise in temperature, weak, bowels move only with oil enemas. Exit.	Onset at 19 with stupor and active symptoms following. Death in about a year. Initial loss of weight which continues, with an afternoon rise in temperature noted in the last month of life. Autopsy –Beneath left 6th rib is a pocket of thick reddish pus. Right apex nodular. Pleura slightly adherent. Death from tuberculosis.

CONDUCT CHART

YEAR	1907
MONTH	7
EXCITED	X
RESTLESS	X
RESISTIVE	X
DEPRESSED	X
APPETITE POOR	X
ILL	X

CASE XIII-17

MENTAL	PHYSICAL	SUMMARY
1907, June—Thought everyone was doing wrong, fault-finding, cries. "A man in front of him in church put an electric bullet through him." December—Dull and sluggish mentally. Dull and subject to anger for past two years. Would not associate with other workmen, gave up jobs without cause. Threatened to shoot himself and his mother. 1908, March—Oriented. April—Untidy.	Often had malaria. 1906—Slight cough noticed. One slight hemorrhage. 1907, June-December—In a Consumptives' Home. Emaciated. December—Anemic, weak, dry, hard cough. 1908, February—Aches and pains, diarrhea, pains in stomach. Dyspnea. March—Decubiti. Slight tendency to clonus in both ankles. Harsh, dry, crackling rales. Dullness at apex. April—Weak, hemoptysis. May 1—Death.	Physical signs became evident before the mental trouble. Course complete in about a year. Autopsy—Shows 75 c.c. of straw-colored fluid in peritoneal cavity. Mesenteric glands enlarged. Lungs adherent throughout. Pus cavity opened in removing sternum, numerous pus pockets in each lung. Ulceration of lower ileum and beginning colon.

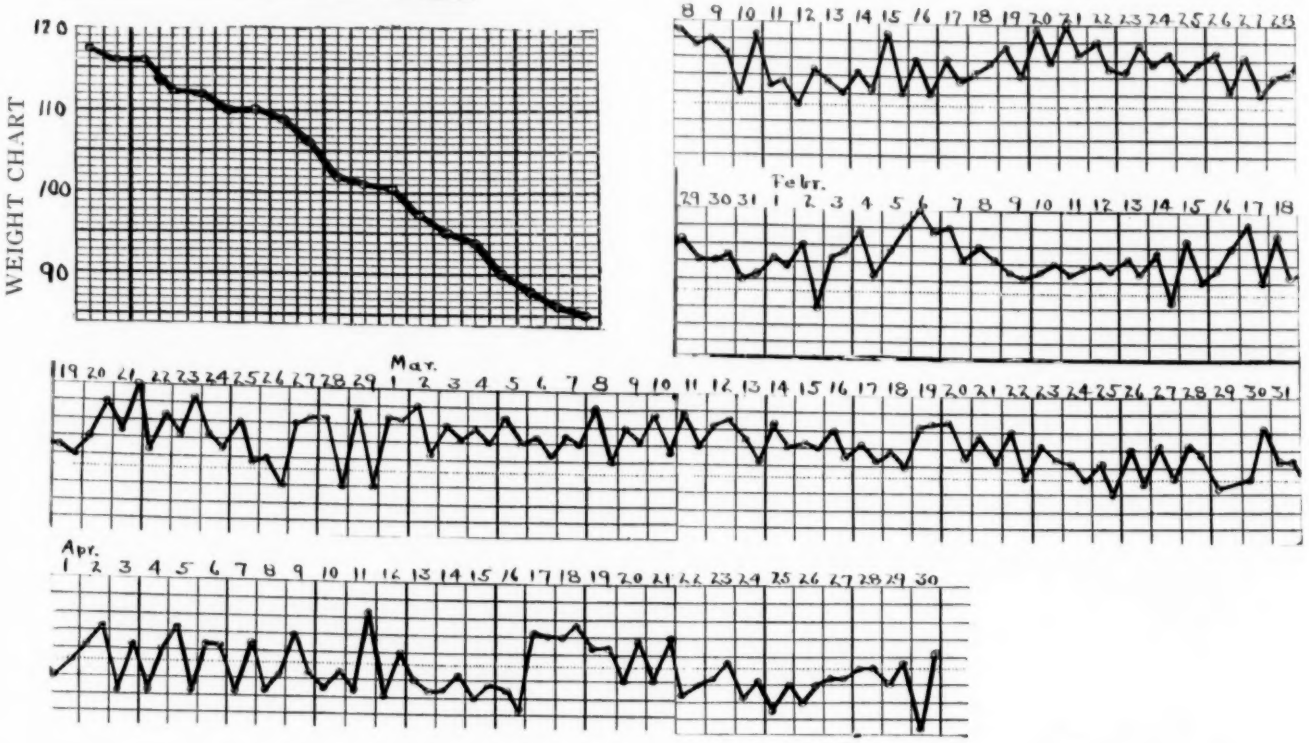
(See Chart, page 416.)

CASE XIII-17

CONDUCT CHART

YEAR 1907 1908

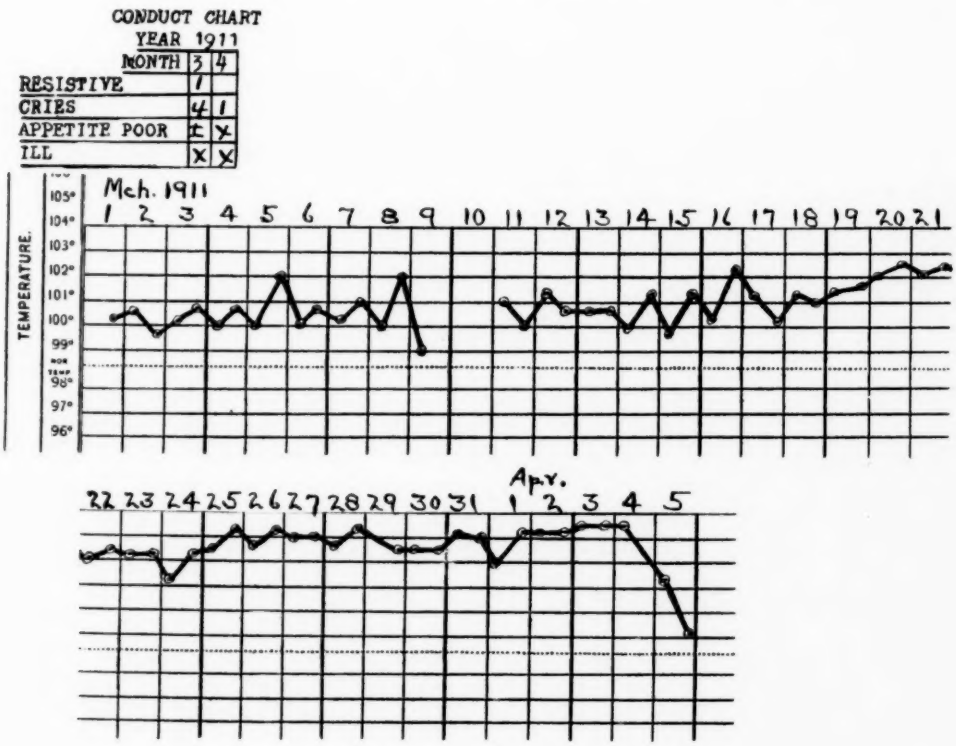
MONTH	12	1	2	3	4
UNTIDY					X
SLEEP POOR		X	±	X	X
APPETITE POOR	±	X	X	X	X
ILL	X	X	X	X	X



(See Table, page 415.)

CASE XVI-23

MENTAL	PHYSICAL	SUMMARY
1907 — Talked and acted strangely. Worse the past eight months. Talks to self, will not eat. 1911, March — Excited, depressed. "I see people around the walls, calling me." Fear affect. "They hit me on the head," "they fire bullets at me," "I am married" (patient is single). Dull, tendency to catalepsy, confused and sometimes apprehensive.	Has been in bed the past five months. Says she does not sleep. 1911, March—Weak, sallow, anemic. Lips and tongue dry. Signs at right apex. Sleeps poorly.	Gradual course of three years, ending with acute mental trouble and signs of tuberculosis. Autopsy — Right pleural cavity contains about 200 c.c. of slightly bloody fluid, left the same amount of puriform fluid. Old fibrous adhesions at apex. Anterior surface seat of thin, plastic, greenish-yellow exudate. Right lung nodular at apex. Left lung apex solid; section shows cavities. In upper and lower lobes are solid areas showing discrete and confluent, yellowish green areas, some with cavities.



CASE XVII-43

MENTAL	PHYSICAL	SUMMARY
1911, August—Onset gradual. Excited. A woman wanted to harm her. Could see her husband on the horizon. Talk rambling and incoherent, restless nights. 1912, March—Noisy and restless nights. Fairly oriented for time, excited "because afraid of another patient." Partial grasp on surroundings, auditory hallucinations at home, no insight. "Has been sick for six months but not mentally." May—Cries and is talkative. June—Resistive to attentions for past six weeks. Mute at times.	1911, August—Poor physical condition, lost weight, anemia, temperature, insomnia. 1912, March—Feels tired. Below and to the left of the lower angle of the right scapula, dullness and bronchial breathing. Back aches and sore inside. Cough. June—Diarrhea lately, loss of weight, temperature at night. Tubercle bacilli in feces. Exit.	Physical condition parallels mental condition in a woman of 33. Exit in less than a year after onset. Autopsy—Decubiti. Old adhesions lower part of right lobe of liver and transverse colon. Right pleural cavity obliterated, left dense adhesions at apex. Scars at apex of each lung. Ileum seat of 13 ulcers which are shallow bright red, not particularly undermined, follow the circumference of the gut and show nodular elevations on the peritoneal surface.

(See Chart, page 419.)

CASE XVII-43

CONDUCT CHART

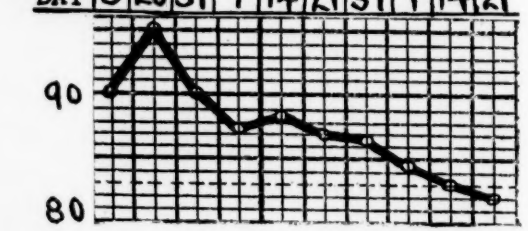
YEAR 1912

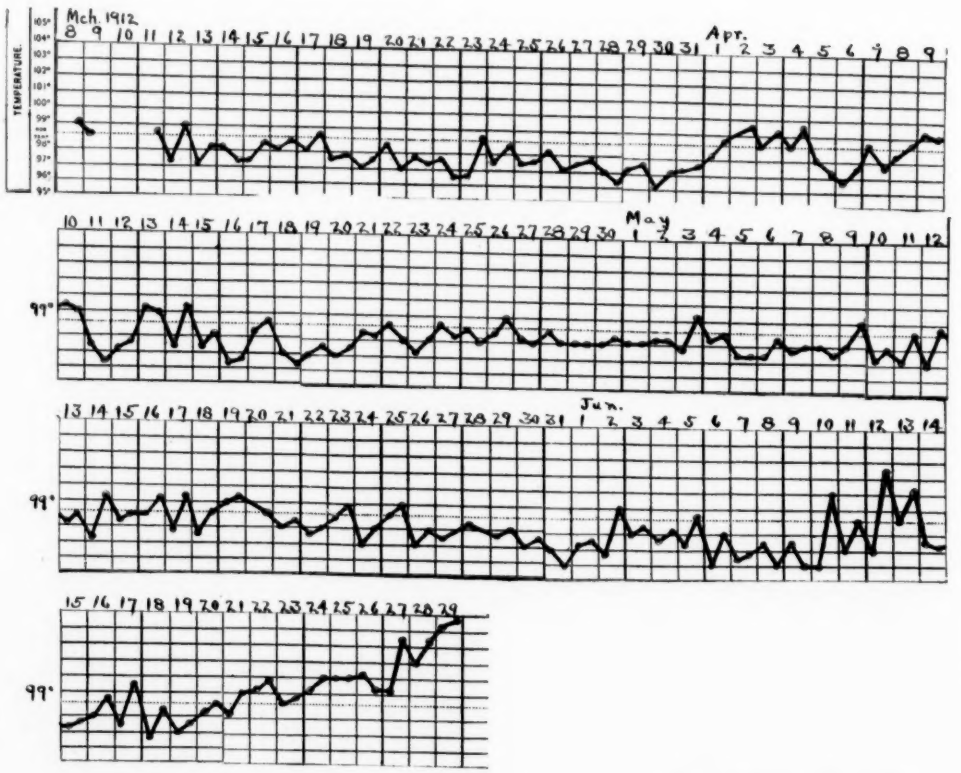
MONTH	3	4	5	6
EXCITED	1			
NOISY		2		4
RESTLESS	2		3	X
RESISTIVE			X	X
DEPRESSED			X	X
UNTIDY			X	X
APPETITE POOR	±	±	±	±
ILL	X	X	X	X

WEIGHT CHART

YEAR 1912

MONTH	MAR.			APR.				MAY		
DAY	8	20	31	7	14	21	31	7	14	21





(See Table, page 418.)

CASE XIV-7

MENTAL

1912, December—Learning new job, got discouraged and gave up suddenly and went back to his old work. Saved his money in a handkerchief under his pillow and occasionally would loaf a few days and spend a little.

1913, February—Ideas of reference, careless in appearance, delusions of persecution, nervous, brooding, silent. Said sister-in-law doped his mother, threatened her. Makes mystic references. Rambling and incoherent at times.

April—Oriented, memory good, reticent, suspicious. Denies all previous actions and statements.

May—Attributes insomnia to poison but shows some uncertainty about it. Sensations of shivering and of difficulty in breathing, "fighting the world all alone." Later aggressive, violent, defiant, threatening, grasp fair, insight none. School knowledge retained. Food tampered with because of its effect upon him. Desires to study the Catholic religion.

1914, January — Hallucinations of sight, hearing and touch explained as the direct work of God. Stares, prays. Twitchings "caused by electricity." Tube fed.

February—Taking food is wrong so will not eat; expels feedings.

PHYSICAL

Father intemperate, apoplexy at 38, died at 41.

1912-'13—Insomnia.

1913, April—Tremor of fingers, knee jerks very active. Wassermann on blood negative.

May—Insomnia.

1914, January—Losing weight.

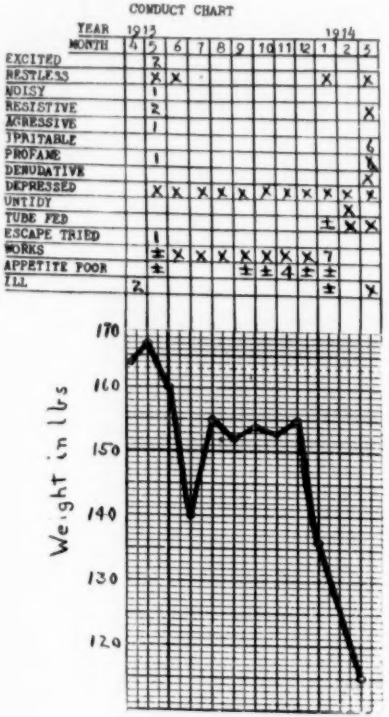
March—Exit.

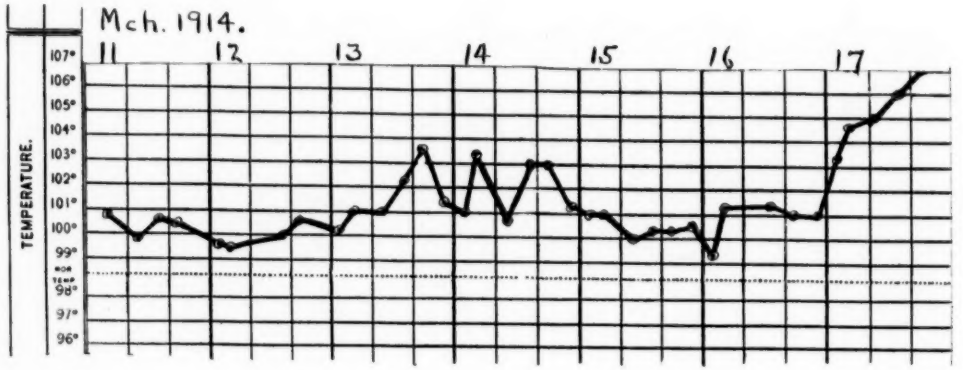
SUMMARY

Duration of active symptoms little over one year. No physical signs discovered at any time.

Autopsy—Right chest contains 30 c.c. cloudy fluid. Fibrinopurulent exudate between upper and middle lobes. Left lung is nodular. Abscess in upper lobe, surrounded by consolidation and many raised, white, coarsely granular areas surrounded by injection.

Duodenum the seat of gray, raised foci. Mesenteric lymph nodes slightly enlarged. Smear from lung positive for tuberculosis.





CASE 1916.25

MENTAL

Did well in school till fifth grade. A poor workman now getting worse. Unsociable, timid, stupid. Recently thought spies were drugging him. Restless, sighs a great deal.

1913, April—Speech disconnected, memory and grasp fair, education poor. Auditory hallucinations recently, references are made to his clothes, etc.; thinks he is drugged to make him drink. Irrelevant at times, insight none. Thought of suicide once. Speaks slowly and in low tones, admits difficulty in thinking.

December—Elopes but returns the next day and says the incident was due to "mental deliriousness."

1914, January—Indifferent, unsociable, memory and grasp good, sometimes evasive, confused, slow in replying, and somewhat irrelevant, has sexual ideas.

August—Oriented, confused, deluded, no insight.

1915, September—Mannerism of hanging head, replies monosyllabic.

1916, March—Restless.

PHYSICAL

Twelve children in family. One died in convulsions, two still-born (the last), one died suddenly at 15, one died of tuberculosis at 25, one insane and suicide, one brother drinks heavily.

Patient had nose-bleeds till 16, then none till last week. Headaches all life.

1913, April—Left back at angle of scapula an occasional rale, pupils react unusually promptly to light.

May—Wassermann on serum suggestive positive, later negative. Right pupil slightly larger than left. Blood pressure 155.

1914, February—Losing weight.

1915, May—Stops work in the Industrial Room, cough, tired, weak, tuberculosis right base, loss of weight, right lateral scoliosis.

June—Sputum negative.

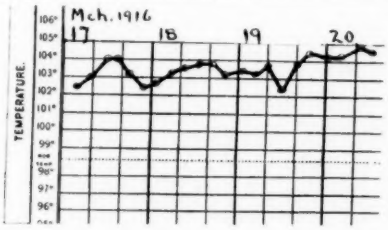
1916, March—Feverish. "Dementia precox sinking spells."

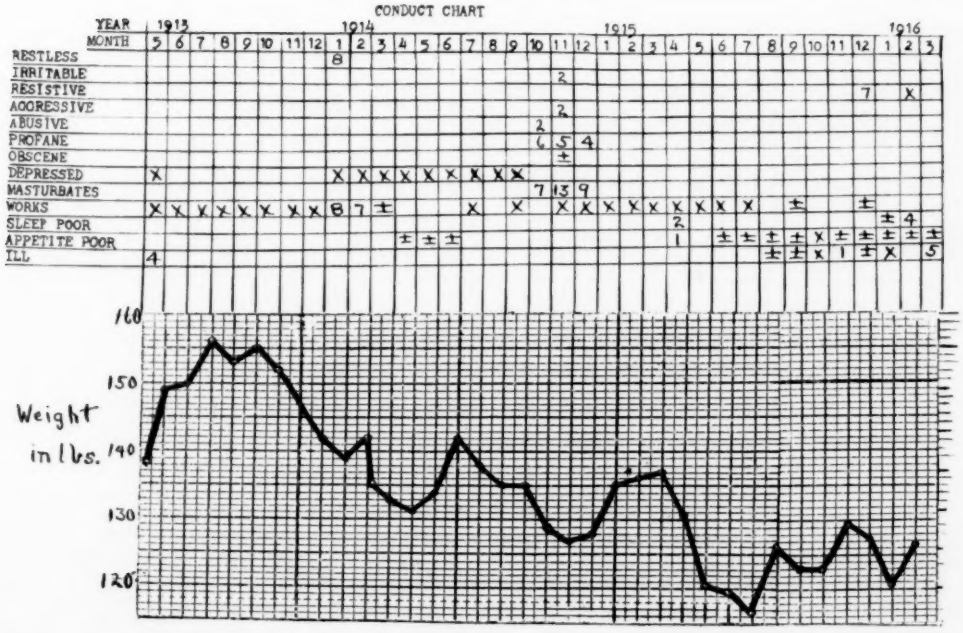
SUMMARY

Gradual onset at 24 leading to admission to the hospital two years later. Here patient remained in a confused and stupid state, though able to do a little work for a time, and died three years later. Physical signs made out almost a year before death.

Autopsy—Adhesions of intestines to ventral abdominal wall, both lobes of liver to diaphragm, spleen posteriorly, gall bladder to hepatic flexure and to small intestine, lungs anteriorly to pericardial sac, right lung at apex, posteriorly over upper lobe and externally over lower lobe, left lung at apex posteriorly and externally throughout. Consistency increased at both apices which are wrinkled and contracted. Rest of lungs nodular and granular. Two small scars left lung. Mesenteric glands much enlarged from behind pancreas down.

Transverse ulcers from middle of ileum down, more frequent at lower end. Small, round, yellow mass posterior to optic chiasm and another large yellow, granular mass in cerebellum, adherent to dura.





great groups from the mental side, independently of the physical picture. By "mental side," of course, one is to understand a combination of the purely mental as determined by mental tests and tests for orientation, memory, etc., and the conduct which is objective, to be sure, but which is an index of what is going on in the patient's mind, especially if considered from the viewpoint of behavioristic psychology. Such a differentiation into a toxic-infection group of catatonic form and a true dementia precox group (if such exist), would be of the utmost importance from the standpoint of prognosis and of rational treatment as against "empirical" treatment. The first would be amenable to treatment or would recover spontaneously but the second would be unfailingly fatal and its elimination would be a matter for preventive medicine, possibly of the eugenics type.

The question of remissions should also be of value in determining to which group any given case belongs. The case with remission should certainly be ascribed to true dementia precox with the greatest hesitation, if at all, if dementia precox is a constitutional dementing psychosis. The fact of remission should point to some other than a constitutional cause.

Turning to the physical side we note that a few cases showed signs of tuberculosis till shortly before death, if we consider only temperature and actual demonstration of the organism. If we review all the data, however, it is evident that tuberculosis might have been suspected in all these cases some time before the diagnosis was made. With present day methods, such as the roentgen rays, sero-diagnosis and other means by special culture media, which are notably few in the insane hospitals of the world and few enough in other hospitals, one might hope to suspect tuberculosis sooner, as we find that we can make the diagnosis earlier. With the continued loss of weight in these cases and the final cachexia one could scarcely make a mistake, but the diagnosis at that time is made too late. The anatomic findings in the lungs of all these cases would have given good roentgenograms long before they reached the stage discovered at autopsy.

Worthy of further attention are the headaches, epistaxis, weakness, the frequency of signs at the apex. Comparing these cases with the previous group we are struck by the frequency of positive findings in the sputum or the feces.

The severity of the lesions may be an index of the clinical course, not only of these cases, but of the cases of the previous paper which seemed, for the most part, to have recovered from the immediate effects of an infection and to have lived out a demented existence only to finally succumb to an exacerbation of the original trouble or to some other infection. An index to the long suspected course of tuberculosis and to the primary locus of infection is also apparent if the locus of lesions in this group is compared with the loci in the previous group. In that former series there were several cases of pulmonary and intestinal tuberculosis and an occasional one with tuberculosis elsewhere. In this present series there were four cases which showed intestinal lesions (XIII-17, XVII-43, 14-7, 1916.25). In addition to the intestine being affected, three of these cases showed enlarged mesenteric glands (XIII-17, 14-7, 1916.25). One case (III-24) showed enlarged glands without apparent involvement of the intestine. Four cases showed involvement of other organs (III-6, III-43, VII-41, 1916.25). This makes a percentage of 47 showing lesions in other loci than

the lung in this series and the percentage in the previous series was 46.1 or somewhat less, though the duration of the disease was longer in every instance in the first series. It is apparent that the pulmonary lesion is of prime importance in point of time and the intestinal lesion follows. Those with intestinal lesions seem to be in the more serious condition since they quickly die and even in the old cases, when intestinal lesions are found, they are fresh pointing to a fresh infection which was the terminal one.

Time appears to have little effect in the spread to the intestine if we are to draw any conclusions of this sort from the above percentages. Neither can we count on the temporal duration in the spread to other organs, though there seems to be some reason for taking time into account here since those cases of the second group (the present paper) which showed lesions in other parts than the lungs and intestines were those with longer duration, from two to four years.

Another interesting speculation is aroused when we consider that the mesenteric glands may be affected without apparent involvement of the intestine and that the abdominal organs may be involved without the apparent involvement of either the intestine or the mesenteric glands. With the assistance of our modern conceptions of infection, local and general resistance, and immunity, a large field for investigation should be opened in the field of psychiatry and tuberculosis which should rival, if not surpass that opened for the studies on paresis.

SUMMARY

Seventeen cases of dementia precox show a mental course and a physical picture so nearly parallel that one is taken to be the cause of the other.

This again opens the question as to the possibility of splitting the great dementia precox group into two main groups on the physical side: those of toxic-infectious nature, often tuberculous, and the true degenerative psychosis. This grouping has nothing to do with the mental groupings.

A wide field for investigation is outlined.

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THE RECENT EPIDEMIC OF INFLUENZA AND BRONCHOPNEUMONIA AT THE EASTON HOSPITAL, EASTON, PA.

Bacterial Findings

A Bacillus Resembling the Bacillus Pestis

By A. L. Kotz, M.D., Easton, Pa.

THE bacterial findings in material obtained from the lungs of 30 influenza and bronchopneumonia patients (mostly bronchopneumonia) either in the form of sputum, pleuritic fluid, lung tissue by aspiration or postmortem, were as follows: The influenza bacillus was found in 15; the pneumococcus (one type or another) in 27; a small diplococcus, forming short chains, in 14; streptococci of various types in 8; and a short thick bacillus in 24. The bacillus is the microorganism to which I wish to draw attention; the other bacteria mentioned have already been more or less thoroughly described by others.

The bacillus is short and thick, about 1.5×0.5 microns, with rounded ends. It occurs singly, in twos and short chains. It is very slightly motile, probably a little more than the ordinary Brownian movement. A capsule is seen in some specimens. Involution forms are common, and are oval, round or irregular. It stains with the ordinary aniline dyes. The ends of the bacillus stain more intensely than the middle. This polar staining is particularly well marked in specimens from the heart blood of inoculated mice stained with Giemsa's stain. It is Gram negative.

The bacillus grows at incubator and ordinary room temperature. On the primary plain agar culture it grows in tiny dew-drop colonies, not unlike the pneumococcus. In subculture it grows in moderately large grayish colonies which are slightly granular. In bouillon culture a moderate cloudiness is produced. If the bouillon is covered with oil after inoculation and allowed to stand undisturbed for a few days, fringe-like filaments develop from the under surface.

This bacillus is highly virulent for white mice. Injection of 0.1 c.c. of a 24-hour bouillon culture into the peritoneal cavity of a mouse kills the animal within three hours. The blood taken from the heart of the mouse contained the organism in large numbers. Mice inoculated subcutaneously with very small doses developed enlarged glands in which numerous bacilli were again found. A culture rubbed upon the shaven skin of a guinea pig produced an infection of the lymphatic glands. Pure cultures were again obtained from these glands.

From the fact that this bacillus is morphologically identical with the bacillus pestis, that it responds to the crucial test of Albrecht and Ghon, and that it is highly pathogenic for laboratory animals, we believe it to be, at least, closely related to the bacillus pestis. Again, from its frequent presence in this disease it would appear to have some significance.

ON THE DETECTION OF SMALL QUANTITIES OF TRICHLOROTERTIARY BUTYL ALCOHOL (CHLORETONE) IN THE FLUIDS AND TISSUES OF THE ANIMAL BODY

By T. B. Aldrich, Ph.D., Detroit, Mich.

CHLORETONE is one of the few organic drugs which (after its administration to an animal) persists as such in the fluids and tissues of the body for any length of time after being absorbed, while its slight solubility in water, its volatility with steam, its comparative stability, and its property of forming needle-like crystals make it possible, under certain conditions, to recognize it readily.

In a previous article *(Journal of Biological Chemistry,* 1918, xxxiv, 263) I have given a method for detecting small quantities of chloretone, either alone or when associated with substances that interfere to a certain extent with its recognition, and which lends itself admirably to the detection of chloretone in the fluids and tissues of the body where few if any disturbing factors are present.

In the stomach or intestinal content, in the urine, or in certain tissues that grind up to a fine pulp, it is only necessary to pass steam through them, but in certain tissues, for example, the blood or serum, it is necessary to subject them to a preliminary digestion with pepsin hydrochloric acid before distilling with steam, since coagulation takes place, and the small amount of chloretone usually present may be prevented from passing over with the steam.

The chloretone may be administered through the stomach in the form of tablets, crystals or capsules or intraperitoneally dissolved in water, oil, alcohol, etc. Both methods of administration may be employed, but regardless of method employed, the animal passes under the influence of the drug very quickly, the rapidity of action being determined by the method of administration, the condition of the dog, etc. The saturated aqueous solution in sufficient quantity works quite rapidly when given through the stomach, the rapidity being influenced by the quantity of food in the stomach, as well as other factors.

In the experiments carried out the dose usually exceeded considerably the M.L.D. of 0.25 gm. per kilo. The smallest dose given was 0.13 gm., the largest 2 gm. per kilo of body weight. Since the dogs were to be killed eventually, an excessive dose could be given without danger, as the animals would live a number of hours even after the administration of a large excess of the drug.

Although chloretone has been recognized in the fluids and tissues of the body only when comparatively large doses have been given, it is to be presumed that it is present and could be detected when small doses were employed, but then only in those organs that have an apparent affinity for the drug.

*From the Research Laboratory, Parke, Davis & Co., Detroit, Mich.

Briefly, the general method of procedure consists in administering to the animal according to weight, a sufficient amount of the drug to produce complete anesthesia, waiting usually from two and a half to three and a half hours (in some cases longer), bleeding from the carotid artery (saving the defibrinated blood), perfusing with saline in order to wash out the remaining blood so far as practicable, removing the organs, reducing them when necessary to a fine pulp, digesting if necessary with pepsin HCl, subjecting to steam distillation, boiling distillate (using a return flow condenser) and examining the lower third of the cooled portion of the condenser for the typical needle-shaped crystals of chloretone.

Although it may not be necessary always to subject the pulp to steam distillation, or to a preliminary digestion with pepsin hydrochloric acid, it is advisable to do this in order to detect the smaller amounts of the drug. When needle-shaped crystals are noted near the crest of the condensing steam, or in the cooled condenser, becoming evident sometimes only after removal of the flame, the presence of chloretone is positive.

The amount of chloretone present has been estimated by comparative tests and is only an approximation.

The following fluids and tissues have been examined: blood, brain, bile, heart, intestine and contents, kidneys, liver, lungs, muscle, pancreas, spinal cord, spleen, stomach and contents, urine and vagus nerves.

One fact stands out very prominently: the nervous tissue, nearly without exception contains chloretone in varying amounts; while it is very frequently absent from the other tissues, and this would lead us to the supposition, which has been inferred but never proved relative to this hypnotic, that the nervous tissue has an affinity for it.

The greater part of the experimental work which follows was carried out a number of years ago when chloretone was first marketed as a hypnotic and anesthetic; but this work was not published at that time. Recently, owing to the wide use of the drug and the consequent new interest aroused in it, it was thought opportune to publish this older data, together with some recent experimental work.

EXPERIMENTAL

A. Recent Work

I. Weight of dog 13.5 kg. (Chloretone administered intraperitoneally.) Sixteen c.c. of a 40 per cent alcoholic solution, or 6.4 gm., given (0.47 gm. per kilo). Dosed 8:00 A.M. (11/8/17) going under in ½ hour. Bled at 8:30, 11/9/17, 80 c.c. of blood being obtained. Organs removed 10:15 A.M., nearly 26 hours after the administration of the drug.

The liquids (blood, stomach contents, and urine) were tested directly by placing in a suitable flask and passing steam through them. When about 100 c.c. of distillate had passed over, it was boiled over a free flame using a return flow condenser. The solid tissues were ground very fine by either passing through a grinder or rubbing up with sand in a mortar and distilled with steam, etc.

It will be noted in this experiment that the dog died 26 hours after the administration of the drug. Presumably most of it had been destroyed.

(1) Brain (wt. 46 gm.)	Positive (slight trace)
(2) Blood (80 c.c. defibrinated)	Negative
(3) Fibrin	"
(4) Liver	"
(5) Lungs	"
(6) Spleen	"
(7) Stomach contents	"
(8) Urine	Very slight trace (?)

II. Weight of dog 8 kg. Chloretone given per stomach; 3.2 gm. of chloretone given in capsules at 1:45 P.M.; at 4 P.M. 2 gm. given in 40 per cent alcohol, intraperitoneally. (0.65 gm. per kilo.)

At 4:10 P.M. dog bled from carotid artery (blood defibrinated). Organs removed two and a half hours after administration of drug.

Method of procedure same as in I.

(1) Brain (wt. 72 gm.)	Positive (½ mg.)
(2) Blood (defibrinated) (300 c.c.)	Negative
(3) Kidneys	Positive (¼ mg.)
(4) Liver	Negative
(5) Lungs	"
(6) Spleen (enlarged)	"
(7) Stomach contents	Positive (30 mg.)
(8) Urine	Negative

III. Weight of dog 7.5 kg. Chloretone given per stomach; 7.5 gm. given in capsules at 10:10 A.M. (1 gm. per kilo.)

Dog was completely under one hour later, and 3½ hours later was bled from the carotid artery, 250 c.c. of blood being taken. Warm saline solution was introduced into the femoral vein until 1200 c.c. had passed through and the wash collected from the carotid artery.

Organs removed 3½ hours after administration of the drug.

The stomach contents and the urine were distilled directly; the remaining organs were ground up and digested with pepsin HCl (250 c.c.) for two days. *Badly decomposed.*

The absence of any chloretone in all of the digested products is attributed to the fact that the flasks being insecurely corked allowed the chloretone to escape, and putrefaction to take place.

(1) Brain	74 gm.	Negative
(2) Blood	150 c.c.	"
(3) Heart	41 gm.	"
(4) Kidneys	21 gm.	"
(5) Liver	240 gm.	"
(6) Lungs	67 gm.	"
(7) Spleen	18 gm.	"
(8) Stomach Contents	50 c.c.	Positive
(9) Urine	60 c.c.	Negative

IV. Weight of dog 11.5 kg. Chloretone given per stomach; 3 gm. of chloretone in aqueous solution and suspension given at 10:20 A.M.

At 10:30 A.M. 5 gm. of chloretone in capsules given (0.7 gm. per kilo).

Dog gradually became completely anesthetized and 3 hours after the last dosing was bled and perfused with about two liters of saline solution. Dog died and autopsy showed that pressure of the perfusing fluid had been so great that it had caused a severe pulmonary hemorrhage.

Organs removed 3 hours after administration of drug. The urine and stomach contents distilled at once; the organs digested.

(1) Brain	Positive (50-100 mg.)
(2) Blood	Negative
(3) Heart	Very slight trace
(4) Kidneys	Positive (very slight trace)
(5) Liver	Negative (accident)
(6) Lungs	Positive (very slight trace)
(7) Spinal cord	Positive (5-10 mg.)
(8) Spleen	Very slight trace
(9) Stomach contents	Positive (300 mg.)
(10) Urine	Negative

V. Weight of dog 9½ kg. Chloretone administered per stomach; 5 gm. given in aqueous alcoholic suspension (250 c.c.) by means of a stomach tube. (0.35 gm. per kilo.)

Was bled from the carotid artery, just three hours after being dosed. The brain, spinal cord, and the vagi nerves were removed three hours after administration of the drug and ground up with sand and each digested with 250 c.c. of pepsin HCl for 16 hours in incubator at 37° C. Worked up in the usual way.

(1) Brain	Positive 20 mg.
(2) Nerves (vagi)	" trace
(3) Spinal cord	" 5 mg.

B. Older Work

VI. Weight of dog 7 kg. Chloretone given per stomach; 300 c.c. of aqueous chloretone solution 0.8 per cent or 2.4 gm. given (0.33 gm. per kilo). Went under in 1 hour. At the end of 2 hours, dog bled from the carotid artery (portion of blood saved) and an unsuccessful attempt made to wash out the residual blood from the body with saline solution.

Contents of stomach and intestine (upper part) were tested directly.

The organs were removed, washed to free them as much as practicable from blood, and then ground up and digested several days with pepsin hydrochloric acid, 500 c.c. of 0.4 per cent HCl and 2 gm. of pepsin (1:3000) being used in each case.

(1) Brain	30 mg. estimated
(2) Blood	40 " "
(3) Heart	5 " "
(4) Kidneys	Slight trace
(5) Liver	" "
(6) Lungs	None
(7) Muscle	Slight trace
(8) Spleen	" "
(9) Stomach contents	500 mg.
(10) Intestinal contents.	400 mg.

VII. Weight of rabbit ¾ kilo. Chloretone given per stomach; 1.5 gm. of chloretone given (2 gm. per kilo). Animal died soon after.

Brain removed and freed of blood as much as possible by washing in water.

Digested in pepsin HCl solution for 5 days. Treated in the usual way with steam, etc.

Brain 10 mg.

VIII. Weight of dog 6 kg. Administered per stomach; 100 c.c. of 0.8 per cent chloretone solution given, or 800 mg. (0.13 gm. per kilo). After 2 hours cannula was inserted into carotid artery and blood washed out as far as feasible from head and brain and the latter placed in refrigerator over night.

One-half of the brain was reduced to a pulp; distilled with steam, etc.

The other half was reduced to a pulp and digested with pepsin HCl (1 gm. pepsin 1:6000) for 4 days.

(1) Brain (direct)	Negative
(2) " digested	40-60 mg.

IX. Weight of dog 11 kg. Chloretone given per stomach; 150 c.c. of 0.8 per cent chloretone solution given: 1½ hours later 250 c.c. more given; finally ½ hour later 250 c.c., 6 gm. in all (0.55 per kilo).

(1) Brain	Crystals of chloretone 10 mg.
(2) Blood	Negative
(3) Heart	"
(4) Kidneys	"
(5) Lungs	"

X. Weight of dog 22½ kg. Given per stomach. Twenty 3-grain chloretone tablets and 500 c.c. of a 0.8 per cent solution of chloretone, 8 gm. in all (0.35 gm. per kilo).

In half an hour dog was completely under. Bled from carotid artery (200 c.c. blood obtained). Stomach and bladder removed.

(1) Blood	Positive
(2) Stomach contents	"
(3) Urine	Negative

XI. Weight of dog 6.4 kg. Chloretone administered per stomach; 320 c.c. of 0.8 per cent chloretone solution or 2.56 gm. total (0.4 gm. per kilo). Killed after 2 hours.

Removed organs after washing out with saline solution.

(1) Brain	10 mg.
(2) Blood	3-4 mg.
(3) Heart	2 mg.
(4) Intestinal wall	Negative
(5) Intestinal contents	0.5 mg.
(6) Kidneys	5 mg.
(7) Liver	10 mg.
(8) Lungs	1 mg.
(9) Pancreas	Negative
(10) Spleen	Negative
(11) Stomach	5 mg.
(12) Stomach contents	150 mg.
(13) Urine	Negative

XII. Weight of dog 9 kg. Chloretone administered per stomach; 350 c.c. of 0.8 per cent chloretone solution or 2.6 gm. (0.29 gm. per kilo) given. Killed after 1½ hours.

Brain removed and worked up in the usual manner. One-half distilled direct with steam; the other half distilled after digestion with pepsin HCl.

Blood and urine were also tested.

(1) Brain	50 mg. (100 mg. total)
(2) Brain (digested)	2.3 mg.
(3) Blood (digested)	5 mg.
(4) Urine tested for acetone	Negative

XIII. Weight of dog 9 kg. Administered per stomach. Had been used for digitalis work. Two hundred fifty c.c. of chloretone solution 0.8 per cent given, or 2 gm. (0.22 gm. per kilo). Killed after 3½ hours.

Brain divided into two portions and treated in the usual manner.

Heart and muscle also tested after digestion.

(1) Brain (digested)	2.3 mg. (4-6 mg. total)
(2) Brain (undigested)	Negative
(3) Heart (digested)	"
(4) Muscle (digested)	1 mg.

XIV. Wt. of dog 9 kg. Administered per stomach. Had been used for digitalis work.

Three hundred seventy-five c.c. of chloretone solution 0.8 per cent given; 250 c.c. given at first, did not go under, later 125 c.c. given (0.33 gm. per kilo). Went under then in a few minutes. In about 5 hours brain removed, ground fine and divided into two portions—one portion was digested in the usual manner. The other portion was treated at once.

(1) Brain (digested)	Positive 5 mg. (10 mg. total)
(2) Brain (undigested)	Negative

XV. Gave dog chloretone in aqueous solution 0.8 per cent 0.2 gm. per kilo of body weight (per stomach). Killed two hours after administration by bleeding. Blood washed out of circulatory system by saline solution before removal of organs. Organs washed also after removal. Blood was saved and tested for chloretone.

Organs ground fine and digested for 48 hours in 500 c.c. of water + 5 c.c. HCl (con.) and 2 gm. of pepsin U.S.P. at a temperature of 38° to 40° C. Each digestive mixture was distilled with steam, etc., in the usual way.

	WEIGHT GM.	CHLORETONE
(1) Brain	59	20-30 mg.
(2) Blood		Negative
(3) Bile		Mere trace
(4) Heart	85	10 mg.
(5) Intestinal walls		100 mg.
(6) Intestinal contents		30 mg.
(7) Kidneys	50	10 mg.
(8) Liver	234	Negative
(9) Lungs	120	100 mg.
(10) Pancreas		Negative
(11) Spleen	37	5 mg.
(12) Stomach		20 mg.
(13) Stomach contents	1900 c.c.	250 mg.
(14) Urine		Negative

XVI. Gave dog same amount as in XV, all conditions same.

(1) Brain	20-30 mg.
(2) Blood	Negative
(3) Bile (did not save)	
(4) Heart	10 mg.
(5) Intestinal wall	100 mg.
(6) Intestinal contents	10 mg.
(7) Kidneys	10 mg.
(8) Liver	Slight trace
(9) Lungs	Negative
(10) Pancreas	"
(11) Spleen	5 mg.
(12) Stomach	2 mg.
(13) Stomach contents	300 mg.
(14) Urine	Negative

XVII. Weight of dog 8.2 kg. Administered per stomach; continual dosage. Four tablets daily (3 grains) 2 in morning and 2 in afternoon or total of 60 grains = 4 gm. (0.50 gm. per kilo).

DATE	WEIGHT	PULSE	TEMP.	DOSE	REMARKS
6/29 A.M.	8200 gm.	96	103.2	6 gr.	
P.M.	8640 "	132	101.4	"	
6/30 A.M.	" "	144	101.4	"	
P.M.	" "	156	101.0	"	
7/1 A.M.	9090 "	168	101.2	"	
P.M.		168		"	
7/3 A.M.	8640 "	120	99.8	"	Weak, does not eat.
P.M.	7730 "	168	104.4	"	
7/5 A.M.	6000 "	136	100.0	"	Does not stand.
P.M.	6400 "	...	101.4	"	
7/6 A.M.		...	....		Found dead.

POSTMORTEM

Dog had been dead overnight and it was consequently difficult to distinguish anything abnormal during life from postmortem signs. Bladder greatly distended, containing 240 c.c. of urine. Acid in reaction. Sp. g. 1.030. Cloudiness, probably mucus or phosphates. The organs were ground up and treated in the usual way after digesting with pepsin HCl.

(1) Brain	1 mg.
(2) Blood	Negative
(3) Heart	Very slight trace
(4) Kidneys	Trace
(5) Liver	Spoiled, not worked up
(6) Lungs	" " " "
(7) Spinal cord	Negative
(8) Spleen	"
(9) Stomach contents	1 mg.
(10) Urine	Negative

XVIII. Weight of dog 5.5 kilo. Chloretone given per stomach; 300 c.c. chloretone solution 0.8 per cent. Anesthetized in 5 minutes. Was killed at the end of two hours by bleeding. Blood saved and organs removed from the body and freed from blood, so far as possible by washing first with saline and then with hydrant water. Digested with pepsin HCl for a few days.

(1) Brain	20-30 mg.
(2) Blood	20 mg.
(3) Heart	1 mg.
(4) Intestinal contents	Negative
(5) Kidneys	3-4 mg.
(6) Liver	Negative
(7) Lungs	1 mg.
(8) Spinal cord	?
(9) Spleen	?
(10) Stomach contents	30 mg.
(11) Urine	Negative

XIX. Weight of dog 11 kilo. Chloretone given per stomach; 600 c.c. of chloretone solution 0.8 per cent given, or 4.8 gm. (0.44 gm. per kilo). Anesthetized in 5 minutes. Remained under all day, sleeping quietly. Killed 6½ hours after drug was given. Bled from carotid artery and vascular system washed out with several gallons of normal saline solution. Dog was still breathing while perfusion was carried on. The organs were thus quite thoroughly washed free from blood. The following organs were removed, further washed with saline solution and tested for chloretone. Each organ was cut into small pieces and digested with pepsin HCl.

It was thought that washing out the organs removed the chloretone, still there was no chloretone found in blood before washing, or the drug may have been eliminated in 6½ hours. *The organs were incompletely digested.*

(1) Brain	Negative
(2) Blood	Negative
(3) Heart	Negative
(4) Kidneys	Negative
(5) Liver	Negative
(6) Lungs	Slight trace (?)
(7) Spinal cord	Negative
(8) Spleen	Negative
(9) Stomach contents	Negative
(10) Urine	Negative

The presence or absence of chloretone in the summary table is indicated by the plus (+) or minus (−) sign. Where the space is blank the organ was not tested; and where a positive sign is followed by a number the latter indicates the estimated amount of chloretone in mg. while the letter (t) or a question mark (?) indicates a trace or a questionable trace. In the fifth column the letter *p* following "bled" shows that the animal was perfused; while in the fourth column "time elapsed" is the time intervening between the commencement of administration and the death of the animal. In II the drug was administered per stomach and intraperitoneally; in I intraperitoneally only; in all others per stomach.

An examination of the table shows that chloretone is uniformly present under varying conditions in the brain and in larger amounts and more constantly than in any other organ of the body, where the organ is taken in its entirety, there being all the way from a trace to 100 mg. or an average of about 24 to 25 mg.

When this measure is applied to the other organs and fluids we find the

SUMMARY

DOGS	WT. IN KILO	DOSE PER KILO	TIME ELAPSED HOURS	MANNER OF DEATH	DIGESTED WITH PEPSIN	BRAIN MG.	BLOOD DEFIBRINATED MG.	FIBRIN MG.	GALL MG.	HEART MG.	INTESTINE (UPPER PART) MG.	INTESTINAL CONTENTS MG.
I	13.5	0.48	26.0	Died	No	+t	–	–				
II	8	0.65	2.5	Bled	"	+0.5				–		
III	7.5	1.00	3.5	"	Yes	–	–			+t		
IV	11.5	0.70	3.0	" p	"	+100	–					
V	9.5	0.53	3.0	Bled	"	+20	–			+5		+400
VI	7.0	0.33	2.0	"	"	+30	+40					
VII	0.75	2.00	1.0		"	+10						
VIII	6.0	0.13	2.0	Bled	"	+60				–		
IX	11.0	0.54	2.0			+10	–					
X	22.5	0.35	0.5	"			+			+2	–	+0.5
XI	6.4	0.40	2.0	" p		+10	+4					
XII	9.0	0.31	1.5		Yes	+100	+5			–		
XIII	9.0	0.22	3.5		"	+3			–			
XIV	9.0	0.50	5.0		"	+10			+t	+10	+100	+30
XV		0.20	2.0	Bled p	"	+30	–			+10	+100	+10
XVI		0.20	2.0	" "	"	+30	–			+t		
XVII	8.2	0.50	84.0		"	+1	–			+1		–
XVIII	5.5	0.43	2.0	Bled p	"	+30	+20			–		
XIX	11.0	0.44	6.5	" "	"		–					
Average number of mg. found						24-25	4.9	t	0	2.5	66	90.1

brain contents is only exceeded by the intestine and intestinal and stomach contents. Here we would naturally expect to find an abundance of the drug (when given per stomach) depending on the amount administered, the length of time before the animal is killed, etc. Leaving these latter out of consideration, we find that the brain contains several times as much as the other organs. Perfusion does not apparently lower the chloretone content of the organs.

In most of the experiments the organs were digested with pepsin hydrochloric acid and this procedure *usually* increased the amount of chloretone obtained. The only exceptions are found in III and XIX where decomposition had taken place during digestion in the former, and where incomplete digestion was found in the latter. In one instance (XII), the half of the brain digested contained less chloretone than the half undigested.

It will be noted that in I only a trace of the drug was found in the brain and none in the other organs. Since the organs were removed 26 hours after dosing, it is to be presumed that the chloretone had been destroyed or eliminated.

In II a portion of the drug was given intraperitoneally dissolved in alcohol and its presence in only a small amount (0.5 mg.) in the brain after 2½ hours is explained by presuming that insufficient time for its absorption had been allowed.

In XVII 84 hours had elapsed which would account for the presence of only 1 mg. in the brain; while when we come to XIX, we find that the organs were very incompletely digested and that a rather long period of time (6½ hours) had elapsed.

In the spinal cord the drug was uniformly present except in XVII and XIX where the reason for its absence can be explained. In the vagi nerves the drug was found positively in V, the only one tested.

TABLE

KIDNEY MG.	LIVER MG.	LUNGS MG.	MUSCLE MG.	PANCREAS MG.	SPLEEN MG.	STOMACH MG.	STOMACH CONTENTS MG.	SPINAL CORD MG.	URINE MG.	V. NERVE MG.	REMARKS
	–	–			–		–		+?		
+t	–	–			–		+30		–		
–	–	–			–		+t		–		Flasks not
+t	–	+t			+t		+300	+10	–		corked tightly.
								+5		+t	(decomposition)
+t	+	–	+t		+t		+500				
		–									
							+		–		
+5	+10	+1		–	–	+5	+150		–		
									–		
			+1								
+10	–	+100		–	+5	+20	+250		–		
+10	+t	–		–	+5	+2	+300		–		
+t					–		+1	–	–		Fed for a
+4	–	+1			–?	+	+30	+?	–		number of
–	–	–?			–	–	–	–	–		days.
2.6	1	9.2	0.5	0	0.9	5.4	130	3	0?	t	

It must be kept in mind also that idiosyncrasy plays a part in relation to this, as well as all other drugs, and may explain some of the variations in amount obtained in the tissues.

The experimental data above emphasizes the fact that the nervous tissue, especially the brain, seems to have a selective action for chloretone which would explain the hypnotic and anesthetic properties of the drug in a large measure. So far as I am familiar with the literature, this is one of the comparatively few instances in which the presence of drugs has been positively proven in the nervous tissues, although this has generally been assumed for a long time, and it is only possible in this case on account of the specific properties of chloretone.

The experimental data raises the question also of the selective action of hypnotics and anesthetics as well as other drugs, but places beyond dispute the selective action of this drug for the cells of nervous tissue, and makes probable the assumption of the selective action of other drugs for the tissues.

BENIGN TUMORS OF THE INTESTINE; WITH A REPORT OF NINE ADDITIONAL CASES*

By G. L. Rohdenburg, M.D.,† New York City

BENIGN tumors of the intestine are of infrequent occurrence, as is shown by Williams,[1] who in 15,481 cases of tumor found the intestine involved but 99 times, an incidence of one-half of one per cent. Of these tumors, 98 were carcinomata and one a sarcoma, no benign tumors being found. King[2], quoting the Mayo reports, states that but 8 cases of true solitary intestinal tumors occurred in the course of 44,654 laparotomies.

The most recent summary, that of King,[2] places the total number of microscopically confirmed cases on record as 124. King's summary is not complete since he has omitted reference to Stetten's[3] two cases of submucous lipoma, and to the latter author's summary of 149 cases of this type. A myoma recorded by Wood[4] is also not mentioned. In addition to these we can recall two cases of fibroma, one reported by Moschcowitz, and another reported by Elliot, both of which were confirmed microscopically; unfortunately, however, the exact references are not available. In addition to King's summary there are several other papers of interest, notably the first collection of cases by Heartaux,[5] and others of more recent date by Dewis,[6] James and Sappington,[7] Voeckler,[8] and one not quite so recent by Adami.[9]

Accepting King's summary as accurate for all practical purposes, we find the various tumor types distributed as follows: fibromata, 16; adenomata, 17; myomata, 45; lipomata, 29; angiomata, 3; teratomata, 2; fibromyomata, 3; neurofibromata, 3; fibroadenomata, 2. Forty-six of these tumors occurred in males, the age periods ranging between 17 and 75 years, while 61 occurred in females, the ages varying between 13 months and 83 years. The distribution in the intestinal tract was as follows: duodenum, 5; jejunum, 8; ileum, 24; ileocecal region, 3; appendix, 1; colon, 22; rectum, 36; vaguely located, as small intestine or intestine, 21. Two things are apparent from this summary; first, that these tumors are more common in the female; second, that they are most common in the rectum and colon. There is no apparent characteristic age incidence.

The clinical symptoms to which the benign growths give rise are of a most indefinite character. Not at all infrequently the growths are accidental finds at operation or autopsy. Occasionally they give rise to vague intestinal symptoms or to intestinal hemorrhage. The most frequent symptom is an intestinal obstruction due either to an actual blockade of the intestinal canal by the bulk of the tumor, or to an intussusception.

Analogous tumors occur in animals, Bullock having observed one such case at the Crocker Laboratory; I am indebted to him for permission to re-

*Of the cases reported in this paper, Cases 1 and 4 were observed in Lincoln Hospital, the remaining seven occurring at the Lenox Hill Hospital.

†Attending Pathologist, Lincoln Hospital and Home, Acting Attending Pathologist, Lenox Hill Hospital.

port this instance in the present paper. The tumor was found at autopsy in a full grown rat and was noted as a localized thickening of the ileum measuring 3 mm. in diameter. Microscopic examination showed it to be a fibroma, which probably arose from the connective tissue of the submucosa (Fig. 1).

While the figures of the Mayo clinic give an indication of the infrequency of these tumor types, using as a standard all abdominal operations, a much more accurate estimate can be formed by considering their incidence in all intestinal tumors. The material available at the two institutions with which the writer is connected comprises 365 intestinal tumors, of which 345 were carcinomata, 3 sarcomata, 8 simple polyps, 3 fibromata, 2 lipomata, 1 myoma, 3 adenomata. Excluding the polypoid growths, there were 9 benign tumors, an incidence of 2.4 per cent. Of the two lipomata in the present series, one occurred in the appendix, and one in the ileum, both being of the submucous variety.

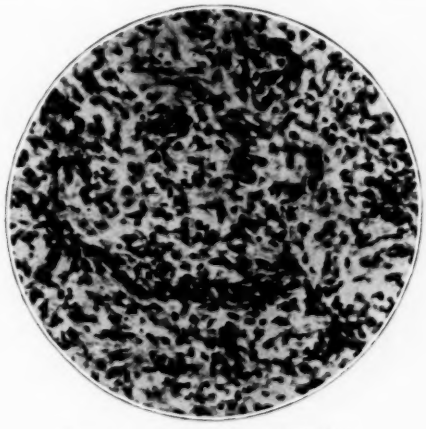

Fig. 1.—Fibroma of rat intestine.

CASE 1.—Service of Dr. S. Erdman. The patient, a male, aged thirty-seven years, was brought into the hospital with a diagnosis of intestinal obstruction. At the laparotomy an intussusception, involving approximately 25 cm. of the ileum at about its middle, was found. The gut was resected and the patient made an uneventful recovery.

Upon opening the removed section of gut, the cause of the intussusception was found to be an encapsulated, soft, yellowish, ovoid tumor measuring 6 cm. in its longest diameter. This growth was situated beneath the mucosa. Histological examination showed a typical lipoma lying between the submucosa and muscularis layers of the intestinal wall. The mucous membrane over it was partially necrotic.

CASE 2.—Service of Dr. F. Torek. The patient, a male, aged thirty-five years, was admitted to the hospital with the history and symptoms usual to an attack of appendicitis. He was successfully operated upon and made an uneventful recovery.

The appendix showed in the gross the common changes of an acute suppurative inflammation, and, upon being opened, showed directly beneath the mucosa 2 mm. from the tip, a circumscribed, yellow, ovoid mass, measuring 4×3 mm. in diameter. This mass upon microscopic examination proved to be a submucous lipoma in which there were marked acute inflammatory changes.

The one case of myoma in the present series occurred in the jejunum.

CASE 3.—Service of Dr. Willy Meyer. A male, aged thirty-four years, was brought into the hospital suffering from a profound anemia subsequent to a violent intestinal hemorrhage. At operation the only discoverable cause for this hemorrhage was a tumor of the jejunum located approximately 30 cm. from the end of the duodenum. The portion of the intestine bearing the tumor was resected and the patient made an uneventful recovery.

The gross specimen consisted of a section of the small intestine 13 cm. in length. About one-third of the distance from the one end, there was an egg-shapped mass with its long axis at right angles to the long diameter of the intestine. The mass, which measured 5 × 3 cm., projected for about two thirds of its bulk beyond the normal intestinal wall and was covered by serosa. The consistency of the new growth was elastic, and section

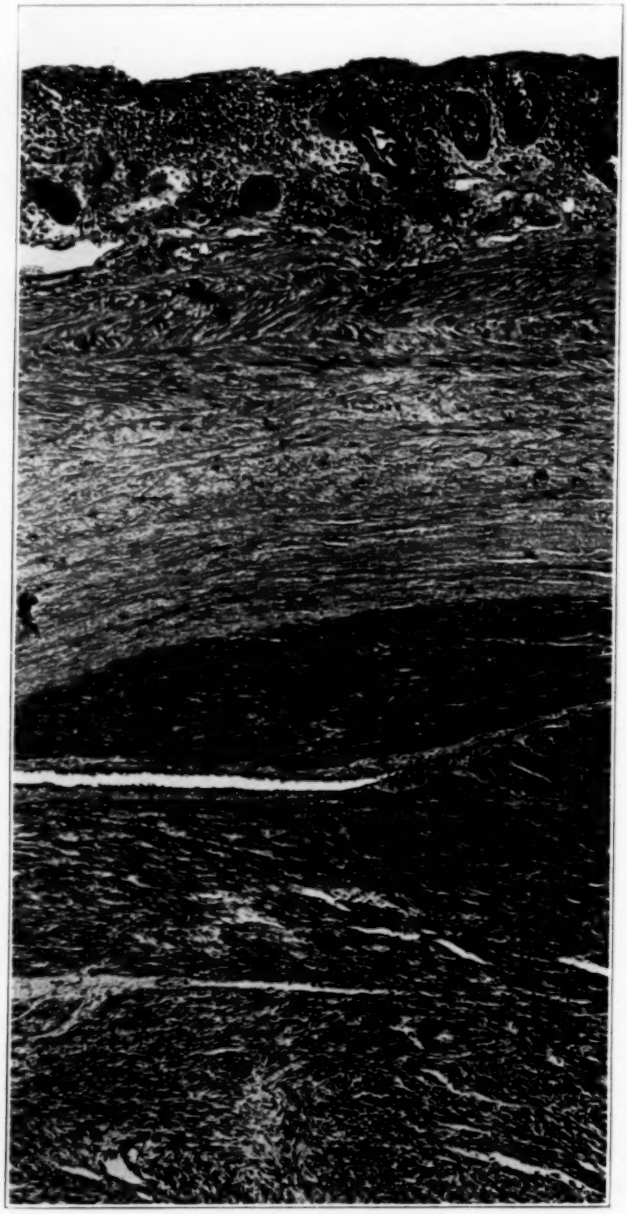

Fig. 2.—Myoma of jejunum.

through it showed it to be of uniform structure and red in color. Microscopic examination (see Fig. 2) showed the tumor to be encapsulated and covered by mucous membrane. The tumor itself was composed of interlacing bundles of smooth muscle fibers, which were moderately infiltrated with polymorphonuclear leucocytes. The tumor had arisen

from the inner layer of muscle, the outer layer though much thinned being still intact.

Of the three fibromata in the present series, one occurred in the rectum, the other two occurring in the ileum.

CASE 4.—Service of Dr. F. Flynn. A female, aged twenty-five years, was admitted to the hospital complaining of intermittent attacks of intestinal hemorrhage, some of which were rather severe. Physical examination showed a pedunculated growth situated approximately 15 cm. from the anus.

The gross specimen consisted of an ovoid-shaped mass measuring 3×1 cm. in diameter. This mass was attached to a small fragment of the rectum by a short narrow pedicle. Microscopic examination showed the neoplasm to be composed of interlacing bundles of connective tissue fibrils with a scanty cellular content. Covering this connective tissue was a somewhat atrophic mucosa which presented areas of ulceration. The entire tumor, particularly just beneath the mucosa, was infiltrated with polymorphonuclear leucocytes.

CASE 5.—Service of Dr. Willy Meyer. This case occurred in a male, aged fifty-two years, who was admitted to the hospital with the clinical symptoms of intestinal obstruction. Upon operation a large portion of the ileum was found to be involved in an intussusception. The intussusception was resected. The patient died of pneumonia five weeks after operation.

The gross specimen consisted of a section of the ileum measuring 70 cm. in length. At about the middle of the section of gut, the wall had been opened and there projected

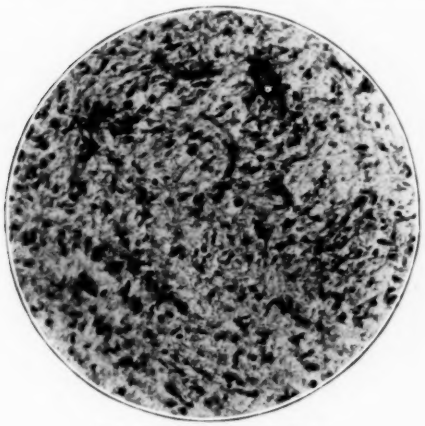

Fig. 3.—Fibroma of ileum.

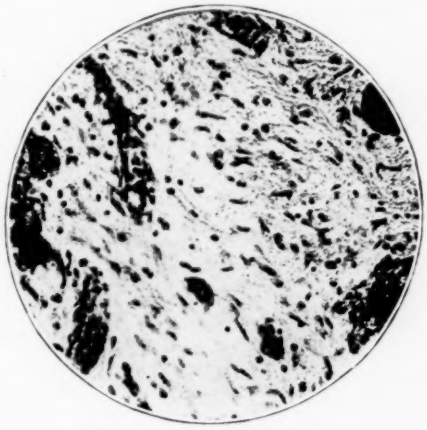

Fig. 4.—Fibroma of ileum.

a pedunculated firm mass, white in color and very resistant to section. This mass measured 6×4 cm. in diameter. Microscopic examination (see Fig. 3) of the growth showed it to consist of a very edematous connective tissue markedly infiltrated with polymorphonuclear leucocytes. Covering the growth was a very much necrosed membrane.

CASE 6.—Service of Dr. Kammerer. This case occurred in a male aged forty years, who was admitted to the hospital with a diagnosis of intestinal obstruction. An intussusception of the lower portion of the ileum was found at operation. After resection of the intussusception, the patient made an uneventful recovery.

The gross specimen consisted of a segment of the small intestine and mesentery, which measured 70 cm. in length. The lumen of the distal, 15 cm. of which was composed of ileum had been incised longitudinally. In this portion of the lumen there was a large pear-shaped tumor approximately 10×6 cm. in diameter. The smaller end or pedicle of the tumor was attached to the wall of the gut 20 cm. from the ileocecal valve. The mucosa covering the tumor was ulcerated. Microscopic examination (see Fig. 4) showed the tumor to be a rather cellular fibroma composed of small spindle and stellate cells separated by a relatively large amount of fibrillar intercellular substance. These were arranged in irregular bundles and in the neighborhood of the blood vessels showed concentric lamellation. The surface of the growth was superficially infiltrated by polymorphonuclear leucocytes. In regions where the mucosa was still present, it rested directly upon the tumor substance which appeared to be directly continuous with the stroma of the mucosa.

Of the three adenomata reported in this paper, two were found in the rectum, and one in the ileum.

CASE 7.—Service of Dr. Oastler. This case occurred in a female, aged forty years, who was admitted to the hospital complaining of rectal hemorrhages. Physical examination showed a growth in the upper portion of the rectum. This was removed and the patient made an uneventful recovery.

The gross specimen consisted of a soft cauliflower-like mass measuring 3×1 cm. in diameter. Microscopic examination (see Fig. 5) showed the growth to be composed of fairly typical appearing glandular acini for the most part straight and lined by epithelium which everywhere rested on a distinct basement membrane. Beneath the epithelial portion, the muscularis mucosa was intact and the submucosa showed no epithelial invasion.

CASE 8.—Service of Dr. Torek. This case occurred in a male of thirty-seven years, who was admitted to the hospital complaining of persistent rectal hemorrhages. A pedunculated growth situated approximately 12 cm. from the anus was found at operation.

The gross specimen consisted of a soft villous mass measuring 5×4×1.5 cm. It was of purplish red color and irregularly divided into lobules. On the surface were numerous long finger-like projections running in all directions. On section the interior contained a narrow core of connective tissue from which the villi projected in all directions. Microscopic examination (see Fig. 6) showed the covering of the villi to consist of an irregular layer of mucous membrane composed of irregular glandular acini and epithelial papillæ. The epithelium covering the papillæ and lining the acini was of the high columnar type and in many places was laid down in several super-imposed layers. The glandular structures

Fig. 5.—Adenoma of rectum.

Fig. 6.—Adenoma of rectum.

were sharply limited to the surface, the connective tissue core in the interior being entirely free from invasion. In the core there was a rather marked chronic inflammatory round-cell infiltration.

CASE 9.—Service of Dr. Stetten. This case occurred in a male, forty years of age, who was admitted to the hospital with a persistent abdominal sinus following appendectomy. At operation the usual appearance of a persistent sinus was found and in addition, a small rounded mass about the opening in the gut. This mass measured 2 cm. in its greatest diameter. Microscopic examination of this mass showed a chronically inflamed granulation tissue on the surface of which were found many irregular gland spaces lined by columnar epithelium which in some places was several layers thick. Some of these glandular spaces were dilated and filled with mucous. The deeper portions of the mass were free from epithelial invasion.

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LABORATORY METHODS

PICRAMIC ACID AS A STANDARD IN COLORIMETRIC DETERMINATION OF NITROGEN BY NESSLER'S METHOD*

By Grete Egerer, Ph.D., and Francis Ford, B.A., Minneapolis, Minn.

THE standard used in Nessler's method of nitrogen determination consists of ammonium sulphate and Nessler's reagent. This standard has the following disadvantages:

1. The ammonium sulphate solution becomes weaker with time, its concentration decreasing noticeably in as short a time as three weeks.

2. Nessler's reagent when prepared according to instructions given in most laboratory manuals on clinical work causes a precipitate in the solution. This, however, can be avoided by using Folin's modified reagent.[1] So far as our tests are concerned the solution never became cloudy when this reagent was applied.

3. The standard frequently begins to darken within eight minutes. A correction for the increase in color of the standard is impracticable as the change is irregular. Direct comparison of an old standard with a fresh one shows an increase in concentration sometimes up to 5 m. in half an hour, at other times showing only an increase of 1 m. in three hours. A standard can be used for only eight minutes with perfect safety. In clinical laboratories where a large number of tests are to be carried out in as short a time as possible, it is a great disadvantage to be compelled to change the standard after two readings.

Accordingly, for clinical work we suggest the blood sugar standard: picramic acid. (Dissolve 0.1 gm. of picramic acid and 0.2 gm. of anhydrous sodium carbonate in 30 c.c. of warm distilled water and dilute to 1 liter.)

This standard has excellent qualities:

1. The color is practically permanent. On comparing a solution of picramic acid made up two years ago with a freshly prepared solution, we found only a slight decrease in concentration, 0.06376 gm. instead of 0.0640 gm. Very likely this difference is due to an inavoidable inaccuracy in weighing. The lapse of time in this instance was greater than in any other test. In other instances the lapse of time was 1, 2, 3, 4, up to 6 months. The result was substantially the same.

2. All color comparisons in which Nessler's test can be used, can just as readily be made by picramic acid.

3. The main advantages are in the saving of time and absence of disturbing factors. During the influenza epidemic we made simultaneous analysis of

*From the Chemical Laboratory, Department of Medicine, University of Minnesota, Minneapolis, Minn.

a high number of bloods. We recognized the great value of the new standard. Our comparisons were made in a Hellige colorimeter. We do not, however, recommend the use of picramic acid as a standard for comparison in the Duboscq colorimeter, because, owing to the greater delicacy of that instrument the range of color tones is much limited. Nevertheless, the colors can be easily matched with a sufficient degree of accuracy in the Hellige colorimeter.

TABLE I

$(NH_4)_2$ SO_4-NESSLER'S AGAINST PICRAMIC ACID

Soln.	1		2		3		4		5		6		7	
	8.5	8.0	15.0	14.5	23.0	23.0	33.0	32.5	40.0	41.5	53.5	52.5	64.0	63.0
	9.0	7.0	14.0	15.0	23.5	23.0	32.5	33.0	40.0	40.5	54.5	53.0	65.0	62.5
	9.0	8.0	15.0	15.5	24.5	23.0	33.5	33.0	41.5	41.5	55.0	53.0	65.5	64.0
	9.0	8.5	15.0	14.0	22.7	21.5	34.0	33.0	41.0	41.0	53.0	53.0	64.0	65.0
	9.0	8.2	14.0	14.5	22.8	22.0	33.5	33.0	42.0	40.5	52.0	53.0	64.0	64.0
	9.5	8.5	14.8	14.5	23.0	22.5	34.2	34.0	42.0	40.0	52.5	52.8	63.0	63.0
	10.0	10.0	15.0	14.0	23.0	22.5	34.0	32.0	42.0	42.0	53.0	52.0	63.1	63.5
	9.0	9.0	15.0	15.0	23.0	21.8	34.0	32.0	41.5	40.5	53.0	52.3	64.0	64.5
	10.0	9.0	14.5	14.0	22.5	22.8	32.5	32.8	42.0	42.0	54.0	54.0	64.5	64.5
Aver.	9.23	8.5	15.02	14.56	22.24	22.55	32.32	32.25	41.49	41.28	51.46	51.77	62.61	63.82
	10.0	8.0	14.0	16.0	23.0	22.0	33.0	30.0	42.0	41.0	54.0	51.5	64.0	65.0
	10.2	8.0	15.0	15.0	22.0	23.0	33.0	32.0	44.0	41.0	53.0	52.0	64.5	64.0
	10.0	8.0	15.2	15.5	22.0	21.0	33.0	31.8	43.0	41.0	52.5	52.0	66.0	66.0
	10.0	7.5	16.0	15.0	22.0	22.5	33.0	32.5	40.0	39.0	52.0	51.0	62.0	62.0
	8.5	9.0	15.0	15.0	23.0	22.0	32.0	33.0	40.0	39.0	53.0	51.0	62.0	62.0
	9.0	8.8	14.8	15.5	22.8	22.0	32.0	32.0	41.0	40.0	53.8	52.2	63.0	63.0
	10.0	8.8	16.0	16.0	23.0	23.0	32.0	31.5	42.0	40.0	50.0	51.0	62.0	65.0
	9.0	8.8	15.0	16.0	22.0	22.5	32.0	31.5	43.0	41.5	52.0	51.0	64.0	64.5
	9.0	9.0	16.0	16.0	22.0	23.0	35.0	31.5	43.0	41.5	52.0	53.0	63.8	64.0
Aver.	9.52	8.44	15.22	15.56	22.42	22.27	31.98	31.81	41.99	40.44	52.55	51.63	63.63	64.00
	10.0	8.0	15.0	15.0	22.0	23.0	32.0	30.0	40.5	43.0	52.0	51.0	64.0	62.0
	8.0	8.0	15.0	15.0	21.0	23.0	31.0	30.0	41.0	41.0	51.0	51.0	64.0	62.5
	10.0	8.0	15.8	16.0	22.0	23.0	32.5	29.5	42.0	41.5	50.0	51.0	63.0	63.0
	8.0	7.5	15.0	14.5	20.0	20.0	32.0	33.0	40.0	40.0	51.0	50.0	63.0	61.8
	9.0	8.0	15.8	14.5	20.5	20.0	33.0	32.0	40.5	40.5	51.0	50.0	63.0	62.5
	9.0	8.0	15.8	14.0	20.5	20.8	32.0	31.0	41.0	40.5	52.0	51.0	63.0	63.0
	10.0	7.5	15.0	14.0	22.0	20.0	30.5	30.0	41.0	42.0	51.0	52.0	61.0	62.0
	9.0	8.0	15.0	15.0	22.0	21.0	31.0	30.0	40.5	40.0	51.0	50.5	60.0	63.5
	9.0	8.0	14.8	15.0	21.0	21.8	32.0	30.0	40.0	40.5	52.0	51.0	60.8	61.5
Aver.	9.11	7.9	15.16	15.16	21.22	21.31	31.77	30.61	40.77	40.99	51.22	50.62	62.42	62.41
Aver. of all determ. made	9.14	8.42	14.83	15.35	22.42	21.85	32.32	31.48	41.49	40.81	51.16	51.20	62.61	62.95

Table I contains three series of readings made with ammonium sulphate solutions of various concentrations. A solution containing 0.7866 gm. in 1 liter was made up. Solution 1 contains 1 c.c. of this stock solution in 50 c.c. Solution 2 contains 2 c.c. in 50 c.c.; solution 3 contains 3 c.c., etc. Three c.c. of the diluted solutions were treated with 2 c.c. of Folin's modified reagent and read against the blood sugar standard.

TABLE II

AMMONIUM SULPHATE-NESSLER AGAINST NESSLER'S STANDARD

Sol. 1		2		3		4		5		6		7	
13.0	13.0	20.0	21.8	32.1	29.5	40.0	39.0	49.5	47.0	60.0	56.0	68.0	68.0
14.0	13.0	20.0	21.0	33.0	29.0	38.5	38.0	49.5	49.0	60.2	57.0	67.5	67.0
13.5	13.5	19.5	22.0	33.5	30.5	39.0	38.5	50.0	48.0	59.0	58.8	69.0	68.5
130.0	13.0	23.0	20.0	32.5	32.0	40.0	36.0	48.5	48.0	57.5	59.0	59.5	66.0
14.0	13.5	24.0	20.5	31.5	30.5	41.5	36.0	49.0	48.0	56.0	58.0	69.5	66.0
14.3	14.0	23.5	20.0	32.5	31.5	42.0	36.0	49.0	48.0	56.5	58.0	69.5	66.0
14.0	14.0	22.0	22.0	33.0	33.5	42.0	39.0	49.0	46.5	56.0	54.0	68.6	66.0
12.5	14.8	21.5	22.8	32.5	32.0	40.0	38.5	51.0	47.8	55.0	54.5	66.5	62.0
13.0	15.0	23.0	23.0	32.5	32.0	39.7	39.0	48.8	48.0	55.2	55.5	67.0	63.0
12.0	12.8	22.0	22.2	30.0	30.0	41.5	38.8	50.5	50.0	56.0	59.0	66.0	61.0
12.5	13.0	21.5	22.5	29.0	30.0	40.0	39.0	51.0	49.0	57.0	58.8	67.0	60.5
13.0	13.0	23.0	22.0	30.5	30.0	39 8	38.2	49.5	48.0	58.8	59.0	65.5	61.0
Average		21.91	21.65	31.12	30.87	40.33	37.66	49.49	48.15	55.3	57.27	66.93	64.58
Av. of all determinations		21.78		30.99		38.99		49.0		56.31		65.75	
Max. read		24.0	23.0	33.5	33.5	42.0	39.0	51.0	50.0	60.02	59.0	69.5	68.5
Min. read		19.5	20.0	29.0	29.0	39.0	36.0	48.8	46.5	55.0	54.0	65.5	60.5
Diff. expressed in mm.		4 5	3.0	4 5	4.5	3 0	3.0	2.2	3.5	5.02	5.0	4.0	8.5

Table II is intended to show that analogous variations of readings occur when Nessler's standard is used. The standard was used for but two determinations. The same solutions were employed as in Table I. The numbers in the last row show that the readings may vary to a considerable extent. The average error amounts to 4.03 mg. and 4.58 mg., respectively, as against 3.48 mg. and 3.21 mg., respectively, in Table I.

TABLE III

TABLE FOR ESTIMATION OF NITROGEN WITH MODIFIED HELLIGE COLORIMETER USING PICRAMIC ACID AS A STANDARD

COLORIMETER READING	MG. N IN 100 C.C. BLOOD	COLORIMETER READING	MG. N IN 100 C.C. BLOOD	COLORIMETER READING	MG. N IN 100 C.C. BLOOD
63	35.18	44	26.77	25	16.42
62	35.75	43	26.29	24	15.91
61	34.33	42	25.81	23	15.40
60	33.90	41	25.24	22	14.89
59	33.48	40	24.67	21	14.19
58	33.05	39	24.11	19	13.48
57	32.63	38	23.55	18	12.78
56	32.20	37	22.99	17	12.08
55	31.78	36	22.43	16	11.37
54	31.35	35	21.86	15	9.96
53	30.93	34	21.30	14	9.19
52	30.50	33	20.94	13	8.42
51	30.03	32	20.02	12	7.64
50	29.65	31	19.50	11	6.87
49	27.17	30	18.99	10	6.10
48	28.69	29	18.48	9	5.33
47	28.21	28	17.97	8	4.58
46	27.73	27	17.45	7	
45	27.25	26	16.94	6	

Table III was calculated from the average of a large number of determinations of ammonium sulphate solutions prepared from pure ammonium sulphate. Calibrated Ostwald pipettes and volumetric flasks were used throughout. The solutions were made up just before use. The temperature of the solutions was kept constant. The comparisons were made with the Hellige colorimeter.

Our findings for nitrogen expressed in mg. for 100 c.c. of blood obtained by comparison with Nessler's standard do not exactly coincide with those of Myers and Fine.[2]

Expressed in mg. N. in 100 c.c. of blood:

2	3	4	5	6	7
12.4-10.01	17.50-15.01	21.75-20.02	27.0-25.22	31.09-30.02	35.61-35

The first figures of each concentration are taken from Myers and Fine. Invariably our findings are lower.

In general the findings with picramic acid as a standard are practically the same as with the ammonium sulphate standard, e. g., solution 4 is found to contain 20.02 mg. when read against Nessler's standard, 19.97 mg. (calculated for 100 c.c. of blood) when compared to picramic acid.

Picramic acid is easily prepared from picric acid by a modified method (Jour. Biol. Chem., 1918, xxxv, 565). The following process for purifying picric acid has been found satisfactory in practice: 100 gm. of Baker's chemically pure moist picric acid are heated in 750 c.c. of distilled water until completely dissolved. To the hot solution 24 gm. of anhydrous sodium carbonate (125 gm. crystalline) are added and the solution is filtered through a folded filter. To the hot filtrate about 5 gm. more of the carbonate are added. The mixture is allowed to cool, then filtered on a Buchner funnel, washed twice with water (10 c.c. each time) while still on the funnel. The precipitate is then decomposed with 250 c.c. of dilute sulphuric acid (diluted 1 to 10) in a porcelain dish, and the residue filtered off on a Buchner funnel, washed twice with water (10 c.c. each time). It is then twice recrystallized from alcohol, 60 to 80 c.c. being used the first time, about 40 c.c. the second time. The yield is about 70 per cent. The entire process takes about two hours.

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A PEROXIDASE REACTION WITH SODIUM NITROPRUSSIDE AND BENZIDINE IN BLOOD SMEARS AND TISSUES

By Lieut. (j.g.) Ernest W. Goodpasture, M.C., U.S.N.R.F.,
U. S. Naval Hospital, Chelsea, Mass.

THE demonstration of a peroxidase reaction within certain white blood corpuscles has led to the view that the presence of this activity is a point of distinction of cells derived from the bone marrow, differentiating them from

the lymphocytic series which do not exhibit this property. The reaction is especially prominent about the cytoplasmic granulations of neutrophilic and eosinophilic polymorphonuclear leucocytes, but seems to be absent within the basophilic cells. This chemical activity has been of use to the pathologist in aiding him to distinguish certain cases of myelogenous leucemia from the lymphatic type, but its application to the study of many problems of hematology, tissue pathology and the biochemistry of oxidization has been limited due, no doubt, largely to the unsatisfactory methods which have been proposed for its demonstration.

Until the methods of Graham were described the study of the peroxidase reaction within cells of smear preparations and tissues was an uncertain and more complicated procedure. The first method proposed by him was an adaptation of the well-known peroxidase reagent alphanaphthol with a counterstain of pyronin, two chemicals which are now scarcely available; and especially for this reason he was led to undertake experiments with other peroxidase substrates, with the result that quite recently he has advocated the use of benzidine for this purpose, his method of application giving more satisfactory results than previous investigations had obtained with this reagent. The technic is simpler than that of the alphanaphthol process, though the brown color reaction is not very striking or clean cut.

The use of these two procedures emphasizes the importance of the test and the desirability of a method simple enough to be used routinely and at the same time yielding uniform and clear results. In certain experiments recently I have devised a method for demonstrating the peroxidase reaction within leucocytes of smear preparations and in sections, which I am convinced will meet these needs; and it involves a chemical test for this activity, which to my knowledge has not heretofore been described, depending upon a color reaction with sodium nitroprusside.

The reagents and counterstain are prepared in a single stock solution of the following composition:

Alcohol 95%	100 c.c.
Sodium nitroprusside	.05 gm.
Benzidine (C.P.) (Harmer)	.05 gm.
Basic Fuchsin	.05 gm.
Hydrogen peroxide	.5 c.c.

The sodium nitroprusside is dissolved in as little water as possible (1 or 2 c.c.) and added to the alcohol; the other ingredients are then included. This stock reagent after some weeks has shown no deterioration in activity, although a slight flocculent precipitate settles out in a few days.

TECHNIC FOR SMEAR PREPARATIONS

Fresh smears of blood or other cellular material are permitted to dry thoroughly on the slide. The reagent is dropped upon it in sufficient quantity to cover the smear which is then allowed to fix for one minute. An equal quantity of water is added. A reaction time of three minutes has been in my experience sufficient. The preparation is finally washed out with water and dried by blotting.

The neutrophilic granules of polymorphonuclear leucocytes are stained deeply blue and are sharply defined. Eosinophilic granules are dark blue about their periphery with a lighter center. Basophilic granules do not seem to react. Fairly numerous and sharply defined granules are stained in the so-called transitional cells, and also in certain mononuclear cells of doubtful classification which with the usual stains would probably be grouped with lymphocytes. Most mononuclear cells show no reaction. Nuclei are stained a clear red, cytoplasm and platelets pink, and red blood corpuscles a smooth buff color. Altogether there is a sharp and pleasant contrast.

TECHNIC FOR FROZEN SECTIONS

Thin sections from tissue preserved in formalin are fixed to clean slides by means of gelatin, a method which I think has not been described, but has been used by me for some time with entire satisfaction. A stock of 2 per cent gelatin is kept in a test tube and melted when needed. A thick coat of it is smeared over one-half the slide and the section floated upon it. The section is blotted and pressed between filter papers, then fixed to the slide with a few drops of 95 per cent alcohol, which immediately hardens the gelatin. The section is then immersed in water and is ready for staining.

It is covered with the stock peroxidase reagent diluted with an equal volume of water. The reaction may be observed under the microscope and usually within three to five minutes the colors are sufficiently deep. The excess of stain is washed off in water, the section dehydrated with acetone, cleared in xylol and mounted in balsam.

The intensity of the stain may be readily varied both in smears and sections by varying the dilution of the stock reagent and the reaction time. Material fixed in formaldehyde and preserved in 80 per cent alcohol for several months reacts as rapidly and strongly as that freshly prepared.

The blue coloring substance resulting from the reaction of sodium nitroprusside and benzidine within cells containing peroxidase is insoluble in the ordinary solvents and seems to be permanent. Although investigations as to its nature and the character of reaction which takes place are incomplete, the method of staining has proved so simple and satisfactory that I feel warranted in describing it at the present time. The technic of application of the method to blood smears will be found quite as simple as that now employed with Wright's stain, and the reagent is sufficiently stable; while the resulting stain gives a preparation from which differential blood counts can readily be made. With a sufficient number of observations, differential counts based upon the presence of this important biological property in certain white cells and its absence in others may prove of more practical worth than those founded upon the morphologic differences exhibited by methods now widely in use.

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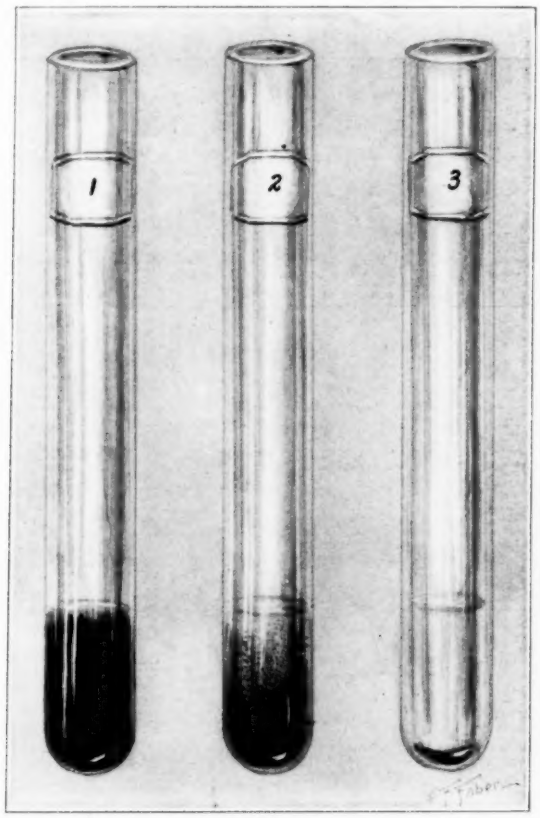
A LEAD PEROXIDE REACTION WITH SPINAL FLUID*

By Edward Steinfield, M.D., Philadelphia, Pa.

LEAD peroxide (PbO_2) is a dark reddish-brown powder, insoluble in water; specific gravity 8.903 to 9.190. A suspension of this compound in distilled water rapidly clears in a few moments, due to settling down of the particles to the bottom of the container. When a suspension is mixed with equal quantities of spinal fluid, the fine particles hold up considerably longer, but ultimately settle to the bottom of the test tube. If the fluid is normal, shaking up the sediment even after twenty-four hours or more, the original appearance



A. B. C.

A.—Normal Fluid.
B.—Case of Tabes.
C.—Meningococcic Meningitis.

of uniform cloudiness is obtained. In pathologic fluids, such as from cases of the various types of meningitis, or syphilis of the central nervous system, a change takes place characterized mainly by adhesion or clumping with attendant precipitation so that on attempting to shake up the tube, large clumps of the metal are thrown about or, as in marked reactions, the entire mass sticks to the bottom of the test tube. This reaction has been applied in a comparative study of normal and pathologic spinal fluids with the result that the phenomenon of

*From the Clinical Laboratories of the Jewish Hospital, Philadelphia, Pa.

LEAD PEROXIDE REACTIONS WITH PATHOLOGIC SPINAL FLUIDS

TEST NO.	NOGUCHI	GORDON'S TEST	CELLS				FEHLINGS	WASSERMANN	BACTERIA	LEAD PEROXIDE	DIAGNOSIS
			TOTAL PER CMM.	POLYS. PER CENT	S. L. PER CENT	L. M. PER CENT					
1	+	±	305	94	6	0	Reduced	Neg.	Meningococci	+++	Meningococcic meningitis
2	+	+	10	21	77	2	Reduced	Neg.	None	-	Fracture of skull
3	+	+	85	84	11	5	Not red.	Neg.	Meningococci	+++	Meningococcic meningitis
4	-	-	280	91	9	0	Not red.	Neg.	None found	++	Suspected epidemic meningitis
5	+	+	40	8	84	7	Not red.	Neg.	Tubercle Bac.	++	Tuberculous meningitis
6	+	+					Reduced	Neg.	Tubercle Bac.	++	Tuberculous meningitis
7	±	±	90	88	10	2	Not red.	Neg.	Pneumococci	+++	Pneumococcic meningitis
8	+	+	35	75	24	1	Reduced	Neg.	None	++	Meningitis (?)
9	+	+	850	91	9	0	Not red.	Neg.	Pneumococci	+++	Pneumococcic meningitis
10	+	+	12,500	95	4	1	Not red.	Neg.	Pneumococci	+++	Pneumococcic meningitis
11	+	+	1170	92	6	2	Not red.	Neg.	Meningococci	+++	Meningococcic meningitis
12	-	-	20	14	84	2	Reduced	Neg.	None	-	Concussion of brain (?) Meningitis(?)
13	+	+	750	90	9	1	Not red.	Neg.	Meningococci	+++	Meningococcic meningitis
14	+	+	480	88	10	2	Not red.	Neg.	Pneumococci	+++	Pneumococcic meningitis
15	+	+	8800	97	3	0	Not red.	Neg.	None	+++	Meningococcic (?) meningitis
16	+	+	860	96	4	0	Not red.	Neg.	Pneumococci	+++	Pneumococcic meningitis
17	-	-	18	16	83	1	Red.	Neg.	None	-	Tetanus
18	+	+	90	11	80	9	Red.	Pos.	None	+	Cerebrospinal syphilis
19	+	+					Red.	Pos.	None	+	Cerebrospinal syphilis
20	+	+	70	15	79	6	Red.	Pos.	None	+	Tabes
21	+	+	160	17	80	3	Red.	Pos.	None	++	Paresis
22	±	±	80	20	78	2	Red.	Pos.	None	+	Early tabes
23	+	+	11,600	96	4	0	Not red.	Neg.	Meningococci	++	Meningococcic meningitis
24	+	+	5400	11	80	9	Reduced	Neg.	Tubercle Bac.	++	Tuberculous meningitis
25	+	+	450	93	6	1	Not red.	Neg.	None	++	Meningococcic (?) meningitis
26	+	+					Red.	Pos.	None	++	Cerebrospinal syphilis
27	±	±	80	11	82	7	Red.	Neg.	Tubercle Bac.	++	Tuberculous meningitis
28	+	+					Not red.	Neg.	Meningococci	++	Meningococcic meningitis
29	+	+	10,400	97	3	0	Not red.	Neg.	None	+++	Meningococcic (?) meningitis
30	±	±	120	13	82	5	Red.	Pos.	None	++	Tabes
31	+	+	8200	96	4	0	Not red.	Neg.	Meningococci	++	Meningococcic meningitis
32	+	+	Blood in fluid				Red.	Neg.	None	-	Fracture of skull
33	+	±					Red.	Pos.	None	+	Cerebrospinal syphilis
34	+	+	1200	96	4	0	Not red.	Neg.	Meningococci	++	Meningococcic meningitis
35	+	+	820	92	7	1	Not red.	Neg.	Pneumococci	++	Pneumococcic meningitis

precipitation has been found to be only present in disease and uniformly absent in normal fluids. The degree of the reaction as measured by the time interval during which it appears and the completeness of precipitation have been of aid in indicating the nature of the pathologic process, as will be shown below.

The test is extremely simple and requires only a suspension of the lead peroxide, a few 5 or 10 c.c. pipettes and test tubes. The suspension is made up in the proportions of 1 gm. of the lead peroxide to 20 c.c. of distilled water and kept preferably in a wide bottle. The suspension is shaken up and 1 c.c. is placed in a test tube (12 × 1.5 cm.). To this is added 1 c.c. of spinal fluid and the whole shaken up for a few moments. The test tube is then allowed to stand in the open air and observed at the end of one-half to one hour and then the next day. The test can also be performed by having a number of test tubes already containing the 1 c.c. of lead and using them as desired. In this way they can be set up at leisure and large numbers of fluids quickly tested when necessary. To observe whether agglutination or precipitation of the lead has occurred, the tube containing the fluid to be tested and one containing a known normal fluid are placed in the same hand and shaken. In this way, the same amount of agitation is brought about in both tubes. The normal fluid will readily become uniformly opaque, the test fluid if abnormal will show some of the following reactions:

1. The particles of lead when shaken up will be coarse and uniform cloudiness of the tube will not occur. Settling takes place gradually.

2. The lead will be in the form of a few large clumps which settle quickly.

3. The lead will form in one clump which may stick to the bottom of the tube and resist shaking; by vigorous efforts it may be dislodged.

In addition, the time element is noted, since early and complete precipitation has been noted in cases of meningococcic and pneumococcic meningitis. The three types of reaction are conveniently designated in order, +, ++, +++. Except in complete precipitation it is well to check up the early observation by the 12 to 24 hour observation. The illustration gives the appearance of the reaction with a normal fluid, with that of a case of tabes, and one of a case of meningococcic meningitis.

The table gives the results with a number of pathologic fluids and a few from cases where meningitis was suspected, with the accompanying confirmatory data. The cell count has been omitted in those examined some time after the tap since it could not be made accurately at this time. About an equal number of normal fluids gave entirely negative results. I am indebted to Dr. Randle C. Rosenberger for a large number of fluids from the Philadelphia General Hospital upon which I made confirmatory observations.

CONCLUSIONS

1. A suspension of lead peroxide is not affected by normal spinal fluids.

2. Varying amounts of precipitation and agglutination occur regularly with abnormal fluids.

3. Early and complete precipitation is observed in the acute types of meningitis.

NEW METHODS FOR PRESERVING SOY-BEAN UREASE*

By G. M. Robinson, M.D., and C. J. Oppenheim, Ph.B., Chicago, Ill.

THE use of soy-bean extracts for the clinical determination of urea is now regarded as a standard laboratory method for rapid and accurate estimations of this substance in the urine and blood.[1] Many methods have been devised for preserving the active enzyme in the dry and wet states; but the former have, in general been unduly complicated, making it necessary to have recourse to clinical laboratories, while the latter have suffered for need of effective preservatives. Hence the clinician still finds it practical to adhere to the Doremus tube with its rather great percentage of error.

At the present time the most popular preservatives for the enzyme in the wet state are those of the toluol series. Toluol makes it possible to preserve the enzyme for about a week, if kept in the ice chest. This, however, necessitates the making of fresh extract at frequent intervals.

Tests have been made in this laboratory on the activity of enzyme extracts made according to the Marshall method[1] and preserved with various preservatives. Those employed were toluol, thymol, eucalyptol, benzol, chlorebutanol, glycerol, chloroform, phenol, ethyl alcohol, trikresol, and camphor. In each case .25 per cent of the preservative was used. The solutions were not placed in the ice chest, but allowed to remain at room temperature and tested at three and four day intervals. The following results were obtained:

Preservative	Number of days before extract failed to convert urea completely incubated at 35° C. for 2 hours or overnight at room temperature.
Phenol	7 days
Ethyl Alcohol	7 days
Trikresol	7 days
Benzol	10 days
Control (no preservative)	10 days
Chloroform	10 days
Toluol	13 days
Glycerol	17 days
Chlorebutanol	17 days
Thymol	17 days
Eucalyptol	20 days
Camphor	? (45 days; still active)

In each case, 2 c.c. of the enzyme converted a weighed quantity of urea (40 mgms.)

From the above tabulations, it may be seen that the preservatives most commonly used keep the enzyme slightly better than ordinarily thought; and without the usual precaution of keeping the preparation in the ice chest. It also demonstrates that neutral gum camphor is much more efficient as a preservative for soy-bean urease than toluol or the other common preservatives.

*From the Pharmacological Research Laboratory, Loyola University School of Medicine, Chicago.

We are able to say that camphor in .25 per cent suspension keeps the activity of the enzyme intact for at least 45 days.

In the hope of securing a permanent wet preparation of the enzyme, glycerol extractions were made with varying quantities of the powdered soy bean. It was found that the following method secured a preparation which answers all purposes and is, to the best of our knowledge, a permanent preparation.

TECHNIC

Twenty grams of powdered soy bean and 100 c.c. of pure glycerol are triturated in a large mortar to complete admixture. This mixture is then transferred to a percolator having a narrow lumen (the ordinary pharmaceutical percolator serves the purpose); and percolated through a layer of glass-wool of approximately one inch thickness for a period of not less than 48 hours. The resultant percolate is of a dark yellow color with a distinctly greenish tinge; and is ready to use after titration for innate alkalinity, *i. e.*, the amount of decinormal HCl required to neutralize one c.c. of the extract. (This need only be done once for the preparation.) This innate alkalinity we have found to be about equivalent to 2 c.c. of the decinormal acid, using methyl orange as an indicator.

One c.c. of the above glycerin extract suffices for ordinary clinical determinations where 5 c.c. of the urine are used. We can see no reason for the addition of acid as usually done in aqueous preparations, since it does not aid in the extraction; nor does it eliminate the necessity for determining the innate alkalinity of the extract. Glycerinized extracts are apparently more active than aqueous extracts of the enzyme, converting more rapidly especially when incubated at 35°C.

It is probable that the above method is equally applicable to extractions of the sword bean and jack bean, which according to Annett[2] and to Mateer and Marshall[3] are decidedly greater than the soy bean in their urease content. These would apparently produce glycerinized extracts of exceedingly high enzyme concentration. The matter is under investigation at present in this laboratory.

SUMMARY

1. The use of .25 per cent neutral gum camphor materially prolongs the period of activity of the enzyme in aqueous preparations of soy-bean urease, without complicating the technic for clinical determinations.

2. Glycerinized extracts of the enzyme afford an active and stable wet preparation which lend themselves readily to clinical procedure.

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A TYPE OF STETHOSCOPE RECEIVING BOWL FOR USE IN THE TEACHING OF MEDICAL STUDENTS*

By John A. Higgins, Chicago, Ill.

THE first practical knowledge that a medical student receives pertaining to the value of the stethoscope in medicine is generally given in the physiologic laboratories. When the period for instructions on the taking of blood pressure in the human begins, at least two known methods of procedure are mentioned. One is that which involves a sphygmomanometer, usually of a Tycos pattern, and a stethoscope, and is generally termed as the sound method. Another method of procedure, which involves a sphygmomanometer of an Erlanger pattern, including a recording tambour and revolving drum, is generally termed as the graphic method.

Where the latter, or graphic, method of procedure is employed in recording blood pressure, it is customary to record the findings on a glazed suface of a smoked drum paper previously gummed on the revolving drum. The blood pressure findings, or graphic tracing, is then interpreted to the students. Following these instructions the students should be able without much difficulty, to make further blood pressure tracings and interpret them.

In the sound method of recording blood pressure we must look upon matters from a different angle. Since an example can not be shown on the appearance of a sound, we must instruct students as best we can regarding what sounds to keep in mind while listening through the stethoscope. The types of stethoscopes ordinarily purchased on the market, no doubt, answer their purpose in the hands of trained medical practitioners. Among the beginning medical students, however, instructors have been compelled to rely upon the student's own decision as to whether or not they actually hear the arterial sounds and whether or not they hear them from the most advantageous areas. Feeling that much gain may be had by having an instructor himself continually listening in on the arterial sounds and also having a number of students listening at the one time, I have designed a new type of stethoscope receiving bowl as shown in Fig. 1. The head pieces that accompany this new type of stethoscope bowl are not changed over the older types but the possibility of four or even more listening from the same receiving bowl is assured.

The stethoscope receiving bowl is constructed by turning down on a lathe from a solid piece of metal, preferably aluminum, a piece similar in construction to piece *A* illustrated in Fig. 2. This piece of metal measures $\frac{7}{8}$ of an inch in diameter on the top surface and 1 inch in diameter on the lower surface. A hole measuring $\frac{1}{8}$ of an inch is drilled through the center. On the lower surface of this piece the drilled hole in the center should terminate into a conical-shaped opening measuring $\frac{3}{8}$ inch deep by $\frac{13}{16}$ inch as the greatest width. Also on the lower outside surface of this piece is threaded a hard rubber band *B*, using No. 32 or less threads to the inch. This hard rubber band sets out about $\frac{1}{8}$ of an

*From the Department of Physiology, University of Illinois School of Medicine, Chicago, Ill.

inch from the lower surface of the metal piece and thus prevents the metal itself from coming in contact with the skin or surfaces placed against. The metal piece at *C* measures 1-$^3/_{16}$ inches in diameter and comes flush with the diameter of the upper surface of the hard rubber band *B*. *D*, which is similar to a metal band permits the lower band *H* of the second section *E* to rest upon the upper

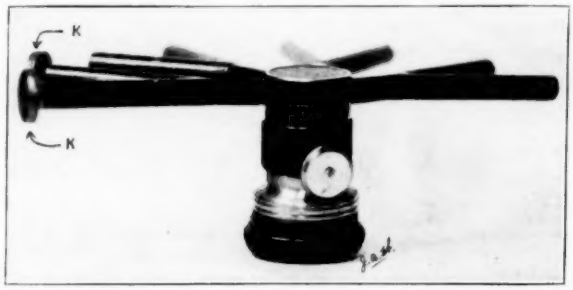

Fig. 1.—Showing a type of stethoscope receiving bowl and the possibility of four or even more listening from the same receiving bowl.

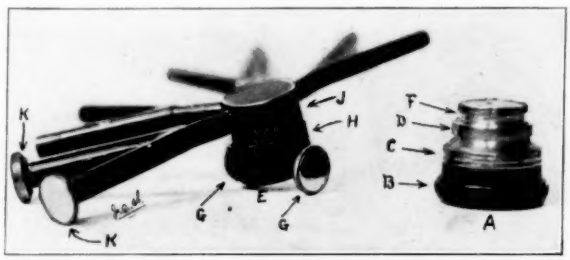

Fig. 2.—Showing the construction of a type of stethoscope receiving bowl.

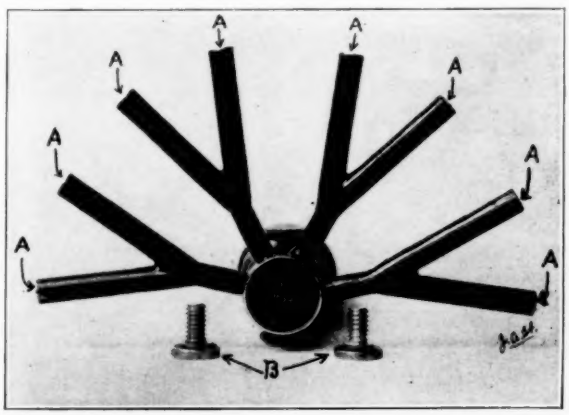

Fig. 3.—Showing top view of a type of stethoscope receiving bowl.

surface and as already shown in Fig. 1. At *F* is a grooved section $^3/_{32}$ inches wide which permits the $^6/_{32}$ threaded screws at *G* to lock sections *A* and *E* together. These screws at *G* need only be long enough to conveniently lock the two sections.

Section *E*, besides the set screws already described, consists of a lower band

of metal *H* 1/16 inch wall by 1/2 inch wide. This band rests on section *A* at *D*. A second metal band, *J*, with a closed top and measuring 3/4 of an inch wide, is soldered into the metal band *H* just far enough so that the lower rims of the metal bands *H* and *J* will rest alternately on the upper surface at *D* and on the top surface of section *A*. On the outer side surface of metal band *J* are screwed in and then soldered firmly four Y-tubes of 1/4 inch brass tube material. This does not mean, however, that only four individuals could listen from the one stethoscope receiving bowl at the one time, because in Fig. 3 is shown ample space for the addition of at least three more Y-tubes. Each Y-tube is connected in turn to the rubber tubes from the ordinary types of headpieces. As long as communication is cut off from the outside, the sounds heard from this type of a receiving bowl do not seem to diminish in clearness.

Where fewer individuals than projecting Y-tubes are to use a bowl of this type, the extra Y-tube or tubes are cut off from outside interference by threading the inside ends of the tubes at *A*, Fig. 3, and screwing in thumb screws *B*, Fig. 3. At *K* in Fig. 1 or 2 is shown a Y-tube thus cut off from outside communication.

While this type of bowl was primarily constructed for use in the physiologic laboratories, its use should not be limited to that field. Its use in the pharmacologic laboratories will permit a comparative study of blood pressure findings upon one another during and after the inhalation of such drugs as amyl nitrite, nitrous oxide, etc.

This type of bowl could also be used in a comparative study of reaction time. This is accomplished by students proceeding to take blood pressure readings from the brachial artery of a subject. Each student listening in on the stethoscope should also be equipped with a signal magnet, dry cell, simple key and a few lengths of copper wire for contact connections. Have each signal magnet arranged to record on a revolving smoked drum, using a rather rapid speed, and preferably a long paper drum. Each signal magnet, so recording, should be directly above one another. Now with the stethoscope bowl resting on the surface of the arm just below where the blood is shut off in the brachial artery, let each student with closed eyes listen for the blood to break through as the tension is removed from the artery. As soon as the first sound is heard let each student independently close the simple key at his command and thus record the first sound. Let some of the same group of students take an alcoholic drink or other mild stimulant and after the stimulant has had an opportunity to react upon the students repeat the experiment together with students under normal conditions, and note any changes in reaction of time. I might also suggest at this point the repeating of this experiment as a comparative study, between students who use tobacco and students who do not use tobacco or other such stimulant. An experiment somewhat along the same basis is already described by Jackson.*

*Jackson, D. E.: Experimental Pharmacology, 1917, St. Louis, C. V. Mosby Co., p. 143, Exper. xiii.

A TYPE OF CONTINUOUS THREADED ANEURYSM NEEDLE*

By John A. Higgins, Chicago, Ill.

THE aneurysm needle,[1] no doubt, seems to be an important instrument in the animal experimental laboratory. Some laboratory workers[2] prefer this instrument in separating muscle borders which thus gives them access to various underlying nerves and blood vessels. Other laboratory workers[3] prefer the threaded instrument in placing ligatures around nerves, blood vessels, or other body tissues. The instrument is also used in raising nerves or blood vessels from a wound while ligatures are placed underneath with the aid of forceps.[4]

In this latter case where forceps are used, in connection with the aneurysm needle in ligating nerves, blood vessels, etc., I am inclined to believe that the main reason the aneurysm needle is not used independently is because of the inconvenience and loss of time in threading or rethreading the present types. Occasions also arise where the loose ligature ends become entangled and thus accidentally separate the ligature from the eye of the needle.

Knowing therefore the value of the aneurysm needle in the experimental laboratory and endeavoring to increase its efficiency as a laboratory instrument I have accordingly designed a new type (Fig. 1).

The advantages offered in this needle are that the ligatures can be carried and kept on wound spools in the upper section of the handle (*A*, Fig. 1 or 2); the needle can be kept constantly threaded, provided ligatures are previously wound upon the spools or new spools of ligatures are inserted in place, using any grade of thread, or mercerized crochet thread, as some investigators may prefer. This will make it quite possible to place two ligatures around a nerve, blood vessel, or other body tissue in one operation. The ligatures passing through a sort of half round, open-faced tubing (*B*) eliminates, to a great extent, the danger of accidentally separating the ligatures from the eye of the aneurysm needle.

The aneurysm needle I shall describe can be made by taking a piece of hard or half hard brass metal measuring 5¾ inches long, ⅝ inch wide, and ⅛ inch thick. Drill a hole, using a No. 47 drill through the center of the ⅛-inch surface and 3/32 of an inch from one of the ends *C*. Cut and file away the metal in a similar fashion as shown at *D* and until the metal piece appears as an ordinary aneurysm needle having the widest flat surface at *E* measure 7/16 of an inch. On the back ⅛-inch surface, solder on a piece of ⅛-inch (outside diameter) brass tubing. File away a section of the ⅛-inch tube wall, as shown between the letters *F* in Fig. 2. This tube should now act as a shield for the ligatures and the filing away of a section of the outer wall should cause no inconvenience in threading.

A second piece of sheet brass metal measuring 4¾ inches long, ⅞ inch wide and 1/16 inch thick is bent into a U-shaped piece with the parallel pieces ⅝ inches apart. This piece is now trimmed down, rounding the corners, etc., and soldered to the end of the aneurysm needle at point *E*, Fig. 1. Two holes are now

*From the Department of Physiology, University of Illinois School of Medicine, Chicago, Ill.

drilled through this piece, using a No. 18 drill. Drill the first hole 3/8 of an inch, and the second hole 1-3/16 of an inch from the end at *G*, Fig. 1. Two round-headed screws of an 8/32 size, measuring 1-3/16 inches long, are taken and on the headed ends are soldered copper burrs, *H*, Fig. 2. These burrs simply reinforce the strength of the screw heads. On the threaded ends of the screws are used 8/32 size screw or lock nuts, *J*, Fig. 2. It is possible at this point, satisfactory, and economic to utilize screw or lock nuts taken from the binding posts of worn-out dry cells, this eliminates time and trouble in turning down the same size nuts on a lathe.

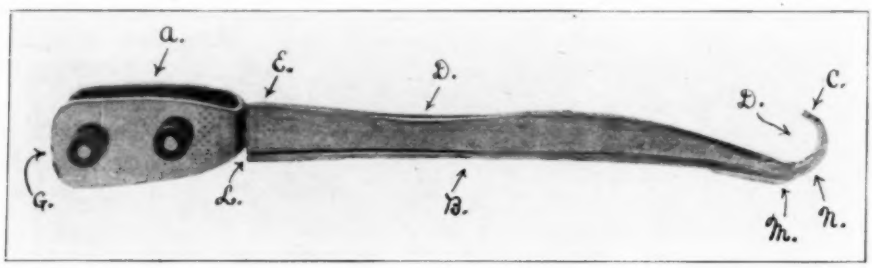

Fig. 1.—Showing a side view of the continuous threaded type of aneurysm needle.

The spools (*K*, Fig. 2) used in connection with this type of aneurysm needle were made from a piece of 3/4-inch hard rubber rod, which spools can be turned down on a lathe to fit into the spool holder. By regulating the lock nuts, *J*, Fig. 2, the friction on the sides of the spools can be increased or decreased at will. The spools in my case were not originally cut out for this particular aneurysm needle and thus necessitated copper burrs between the brass sides of the spool holder and the spools themselves. The spool holder will accommodate the wooden spools

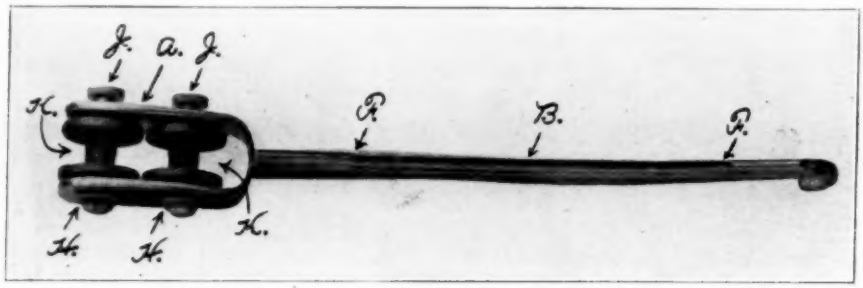

Fig. 2.—Showing a rear view of the continuous threaded type of aneurysm needle.

purchased on the market, which spools, as a rule, contain ten yards of silk thread. The advantage in this instance is that the spools purchased, already wound with thread, saves time in the rewinding of specially made spools. This size of aneurysm needle already described was originally aimed for mammalian work, smaller sizes for amphibian work can, of course, be made accordingly.

In threading the aneurysm needle, the ligatures after leaving the spools, pass through the tube opening at *L*, Fig. 1; past the tube opening at *M;* through the drilled hole at *N*, which hole was originally a part of hole *C*, and through the hole at *C*. Then to operate, after once threading the needle, raise the nerve,

blood vessels or other body tissue in the usual fashion as with the older types of aneurysm needles, procure a hold on the protruding end of the ligature or ligatures and remove the aneurysm needle in a careful manner. When you have secured the length of ligatures desired cut the threads about ¾ to 1 inch beyond the eye of the needle, which thus leaves the needle rethreaded for further ligations.

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EDITORIALS

Encephalitis Lethargica

UNDER the term encephalitis lethargica is included a series of cases observed in England, France, Italy, South America, and recently in the United States, in which the predominant symptoms are connected with the central nervous system. The distinctive features seem to be those of an acute general disease associated with a condition of languor, apathy, and drowsiness passing into lethargy; progressive muscular weakness passing into complete disablement; and a combination of various cranial nerve palsies, of which ptosis, squint, and nystagmus are characteristic signs. From the fact that the ocular muscles were so commonly involved, the disease has been called infectious ophthalmoplegia. Also, and because the disease has been supposed to be connected with food poisoning, it has been thought to be an expression of botulism. It has likewise been called epidemic stupor, acute polioencephalitis, bulbar paralysis, and Heine-Medin disease.

The suspicion that the disease is due to botulism has not been confirmed. In fact the investigations of the Local Government Board on Public Health

seem completely to eliminate this possibility, which had been so prominent. The investigators were unable to find the pathogenic organism and were unable to find evidence in serologic experiments of any suggestion of the presence of the bacillus of botulism. Histologic studies indicate an acute infection rather than an intoxication. Botulism is afebrile; this new disease is febrile.

Moreover, the studies of various men seem to show divergencies from the clinical and histologic picture of poliomyelitis that make it probable that the disease is a new one and not a mere modification of an old. And yet the lesions of the central nervous system resemble to a certain extent those found in general paralysis, syphilis, sleeping sickness, and acute poliomyelitis. Animal experiments also support the evidence that encephalitis lethargica is distinct from poliomyelitis, for inoculations into monkeys failed to produce paralyses. As a whole the findings to date are not satisfactory, but they point to the probability that encephalitis lethargica is a disease anatomically and clinically distinct from all others.

From the practical standpoint it has been suggested, says the Journal of the American Medical Association, that the appearance of this disease has been associated with a breakdown of immunity. Lowered resistance to a usually harmless saprophyte or a "conditional" parasite may be conceived to permit harm to arise from organisms ordinarily harbored with impunity. It is worth the mention that in the French epidemic there was a mortality of 50 per cent. In the series of cases reported by Porthier there was not a death. The reports from Camp Lee, Chicago and New York suggest the possibility that other cases may appear at other places in this country. So far all the cases in America have been in soldiers. This has not been true in England, though it has been the rule. Many of the cases have followed influenza.

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—*P. G. W.*

The Mechanism of Renal Excretion

THE physician who is seeking a knowledge of the function of the kidney in order to better interpret renal disease is quickly lost in the multitude of facts which rival hypotheses have gathered for their support. The modern text book of physiology is unable to give a review of the facts which are presented on literally thousands of pages of published researches, and the physician has never had a "close up" view of the subject. For this reason it is a great delight to take up the recent monograph on the Physiology of Renal Excretion, by A. R. Cushny of the London University.* For this book he has carefully sifted the enormous literature of the subject, and in a remarkably clear and entertaining style written

*Cushny, A. R.: Secretion of Urine, Longmans, Green & Co., London, 1917.

in a personal manner of the problem. Out of the tangled mass of facts presented by the literature he has evolved what he terms a "Modern Theory of Renal Excretion." He believes that this theory best explains the now known facts of renal function and that it will serve as a help in the understanding of renal disease.

The great number and the variety of substances which are found in the blood and the urine make it seemingly impossible that urine excretion depends on chemical combinations within the renal cells, and suggests a physicochemical mechanism to explain the phenomenon. The problem of how the kidney fabricates a highly concentrated solution of salts from a dilute solution of the same salts in the blood plasma is complicated by the fact that the ratios existing between the concentration of each urinary salt in the urine differs from that present in the blood. The urine is not a deproteinized blood plasma.

While it has not been possible to determine the nature of the forces which operate, it is possible to postulate that they function by one of two mechanisms. The one is that the urine is a filtrate of the blood which has passed through a portion of the renal epithelium into the tubules as a very dilute fluid, i.e., a deproteinized blood plasma and that the dilute fluid is concentrated by the absorption by physical chemical forces of fluid and salts by other cells of the kidney and replaced in the blood. The other mechanism would have it that the salts and the water are each actively excreted by the various cells of the renal epithelium. The first is known as the physical theory, and the second the vital theory of urine excretion. Both of these theories are inadequate to explain the phenomena which research has shown to occur in the kidney, but they have served to develop what Cushny terms "the modern theory of urinary excretion."

This modern theory accepts the general scheme of filtration and reabsorption of the physical theory, but pays due respect to the fact that the known physical forces are not adequate to explain the reabsorption which must take place to produce the concentration of salts found in the urine. It, therefore, supplements the physical theory by assuming a vital activity on the part of the epithelium of the tubules in reabsorbing fluids and salts from the dilute filtrate coming from probably the glomerulus and capsule. In short, Cushny's modern theory is as follows:

A large amount of blood plasma fluid is filtered through the glomerulus into Bowman's capsule, the filtering force being found in the blood pressure. This fluid has the same concentration of the salts to which the capsule is permeable as does the blood plasma. The blood leaving the glomerulus is, therefore, a somewhat concentrated solution of plasma colloids, and must have returned to it the proper amount of fluid and salts to make it an optimum fluid for the body cells. This is accomplished by the active absorption of a part of the glomerular filtrate by the cells of the tubules. The salts which are of no use to the body are not reabsorbed and, therefore, appear in highly concentrated form in the urine. These salts are termed "nonthreshold substances," and since their presence in the plasma is unnecessary, they continue to be excreted as long as they are present in the blood. The salts which are necessary are termed "threshold substances," and are reabsorbed until they are again present in the blood plasma in the optimum amount. For example, urea continues to be excreted as long as there is any present in the blood, while glucose is completely reabsorbed so long as its concentration remains under a more or less fixed level.

Although it is quite impossible to develop here the argument which Cushny finds in favor of the modern theory, mention may be made of the best experimental evidence supporting it, inasmuch as a portion of it has a clinical significance. For example, he calculates that to produce 1200 c.c. of urine containing 20 grams of urea, 60 liters of blood plasma fluid containing 0.03 per cent urea would have to be filtered through the capsule and 58.8 liters of water returned to the blood by the uriniferous tubules. Since the blood flow through the kidneys is very great, amounting to about 500 liters per day, only about 13 per cent of the fluid contained by the blood passing through the glomerulus would pass by filtration through the capsule of Bowman. This seeming large amount of water which the tubules would have to reabsorb per day is small when it is pointed out that because of the great number of these tubules each would probably not have to reabsorb more than 0.01 c.c. per hour.

The modern theory assumes that the capsule is a filter which allows the deproteinized blood plasma to pass through it into the renal tubes. The passage of the fluids through the membrane would depend upon several factors:

First. The difference in the pressure between the blood and the urinary filtrate. This is furnished by the pressure of the blood in the glomerular vessels.

Second. The character of the membrane of the capsule. The capsule is impervious to the proteins of the blood and pervious to its other constituents.

Third. The character of the blood. If the blood contains a substance which can not pass through the filter and which exerts an osmotic pressure in opposition to the filtering force, it will act to reduce the rate of filtration as well as the amount filtered.

If the capsule acts as a filter it should be possible to alter the rate of urine excretion by varying any of these factors, and such is the case. For example, if the blood pressure be raised by tying off several branches of the aorta, the urine is appreciably increased, or if the blood pressure is decreased, as can be done by compressing the renal artery, the amount of urine is decreased. Increase in blood pressure alone without at the same time increasing the volume flow of blood through the kidney apparently does not increase urine excretion. This is explained by the fact that any notable increase in the concentration of the colloids in the plasma increases the osmotic pressure of the blood which acts in opposition to the pressure of blood in the capillaries. This point was shown a number of years ago by Starling and his pupils who found that the secretion of urine ceases when the capillary pressure in the glomerulus falls below that exerted by the osmotic pressure of the blood proteins, the critical pressure being from 30 to 40 mm. of mercury. They also found that when the osmotic pressure of the blood proteins was reduced by dilution of the blood with saline solution, the rate of excretion was increased; excretion in such cases being maintained at a blood pressure below the normal critical pressure. If the dilution of the blood was made with saline containing gelatin, on the other hand, the diuretic effect was greatly decreased. These experiments indicate that saline produces its diuresis by diluting the plasma proteins and lowering their osmotic pressure. The proof that the capsule acts as a filter appears fairly complete, but no such experimental evidence can be obtained to prove the assumption that the

epithelium of the tubules reabsorbs the excess water and salts which are filtered off through the capsule.

If Cushny's modern theory of excretion is correct, the tubules must absorb not only large amounts of water, but they must allow for the reentrance into the blood, either completely or incompletely, of certain salts while they must reject others entirely.

The urine contains a very high percentage of small molecules, and the proportion in which they are present is entirely different from that found in the blood plasma, and, presumably, in the glomerular filtrate. The following figures give the average normal value for urea, uric acid, chlorine and glucose in 100 c.c. of protein free blood plasma and 100 c.c. of urine, in the third column is given the change in concentration which occurs in the kidney:

	100 C.C. PROTEIN-FREE BLOOD PLASMA CONTAINS	100 C.C. URINE CONTAINS	CHANGE IN CONCENTRATION IN THE KIDNEY
Urea	.033	2.	60
Uric Acid	.0022	.05	22.7
Chlorine	.41	.6	1.5
Glucose	.1	-	-

Here the blood plasma fluid contained but 0.033 per cent of urea, and the urine 2 per cent. Accordingly, 6 liters of glomerular filtrate would be required to furnish 100 c.c. of urine. Six liters of glomerular filtrate would contain 6.6 grams of sugar, 0.132 grams of uric acid, and 24.6 grams of chlorine. But 100 c.c. of urine contains no glucose, 0.05 grams of uric acid and 0.6 grams of chlorine. According to the modern theory, these figures indicate that during the passage of the urine through the tubules 5900 c.c. of water, 6.6 grams of sugar, 24 grams of chlorine and 0.067 grams of uric acid would have to be absorbed by the renal epithelium in the production of 100 c.c. of urine containing the concentration given above.

Among the most convincing experiments that can be offered in support of the absorption of fluid and salts by the tubules are those in which the pressure of the urine in the tubules is slightly increased by partial closure of the ureter (Cushny). In these experiments the ureter of one kidney is partly closed with a clamp and the excretion obtained from this kidney is compared with that of the opposite normal kidney. In general, obstruction of the ureter results in a decrease in the amount of water, chloride and urea excreted. But, curiously, the urea content is decreased relatively less than is the chloride and water content. These results can be explained on the basis that any pressure acting to oppose the head of pressure producing filtration in the glomerulus will reduce the amount of the glomerular filtration, and accordingly the time allowed for the passage of this filtrate along the tubules is increased, and absorption becomes more complete. Since urea is probably not absorbed at all and chloride is, the discrepancy in the effects on the excretion of urea and chlorine in the partially obstructed kidney can be explained.

When very large amounts of water are taken by mouth, it often happens that the urine excreted has a concentration of salts less than that present in the fluid of the blood. Some investigators believe that such a condition is possible

only on the assumption that water is actively excreted, but a more plausible explanation based on the modern theory is that the water that is absorbed from the alimentary tract reaches the kidney as a dilute saline solution, and is rapidly filtered off in a form somewhat more dilute than the optimal solution which blood plasma must have for the well-being of the tissues.

It is impossible to analyze the forces that are responsible for such a degree of absorption by the epithelium of the tubules. For the present we must classify them, for want of a better term, as vital forces. The questions that await immediate investigation are whether absorption actually takes place, and, if it does, what factors cause it to vary. Many attempts have been made, by destroying the capsules or the tubules by means of poisons or by operations to determine directly or indirectly the question of the function of the tubules.

In such experiments, however, the number of factors involved confuse the issue and make the results practically valueless so far as determining the normal function of the tubules. Other experimenters have attempted to show absorption in the tubules by injecting diffusible substances, such as chemicals and dyes, into the ureter under what they deemed sufficient pressure to force the solution into the tubules, and by an examination of the blood or the tissues to determine whether or not the injected substances had been absorbed. The results obtained are not convincing, for it is very questionable whether it is possible to inject a substance into the tubules from the ureter.

Cushny fails to find any evidence for the vital theory of excretion in the supposed ability of the renal cells to excrete dye substances injected intravenously. He points out that all well controlled work has failed to confirm this generally accepted teaching. Cushny gives the accompanying table in which the movements of the concentration of the blood plasma are followed through the kidney. The ultimate destination of each is indicated by the enclosures. It is noted that the dextrose alone is completely absorbed and that the urea and the sulphate are not absorbed at all from the glomerular filtrate. The other salts are partly absorbed.

	67 LITERS PLASMA CONTAIN		62 LITERS FILTRATE CONTAIN IN ALL		61 LITERS REABSORBED FLUID CONTAIN		1 LITER CONTAINS	
	PER CENT	TOTAL			PER CENT	TOTAL	PER CENT	TOTAL
Water	92	62.1	62.1		—	61.1	95	950 c.c.
Colloids	8	5360 gr	—		—	—	—	—
Dextrose	0.1	67 gm.	67	gm.	0.11	67 gm.	—	—
Uric Acid	0.002	1.3 "	1.3	"	0.0013	0.8 "	0.05	0.05 gm.
Sodium	0.3	200 "	200	"	0.32	196.5 "	0.35	3.5 "
Potassium	0.2	13.3 "	13.3	"	0.019	11.8 "	0.15	1.5 "
Chloride	0.37	248 "	248	"	0.40	242 "	0.6	6.0 "
Urea	0.03	20 "	20	"			2.0	2.0 "
Sulphate	0.003	1.8 "	1.8	"			0.18	1.8 "

He points out that Barcroft and Straub have shown that the diuresis which results from the injection of saline into the blood is not accompanied by any in-

crease in the oxygen consumption of the kidney, and that this fact coupled with the fact that the total amount of chloride, urea and sulphate, which is excreted during saline diuresis is greater than under normal conditions indicates that the excretion of these salts is not due to any vital secretory power of the kidney, but rather to factors that are extrarenal in origin.

The diuresis produced by adding urea or sodium sulphate to the blood, on the other hand, is accompanied by an increase in the oxygen consumption of the kidney. This increase can not be due to active elimination of these salts by the tubules, the work of which requires oxygen, for no increase in oxygen consumption accompanies the increased excretion of the same salts under saline diuresis. Sulphate and urea are nonthreshold substances, and are not absorbed by the tubules. The explanation of the oxygen consumption is probably that the osmotic pressure which these bodies in the glomerular filtrate exert makes it necessary for the epithelium to oppose a greater absorbing force to concentrate the urine, and hence a greater expenditure of energy is required.

While the modern theory does not explain the diuretic action of the xanthine compounds, it does allow for the explanation of the polyuria in diabetes, this polyuria being due (1) to the excessive amount of water taken, and (2) to the inability of the kidney to concentrate the urine against the osmotic pressure offered by the concentrated sugar solution in the tubules. In these cases sugar is a nonthreshold substance, so to speak, and none of it is absorbed. The diuretic action of the digitalis group is dependent upon its influence on the circulatory system. The diuretic action of pituitary extract has not been determined in the light of modern theory. The presence of albumin in the urine in nephritis and cardiac failure would be explained by the modern theory as being due to a change in the permeability of the filtering membrane. —*R. G. P.*

*Acute Infectious Jaundice**

EPIDEMICS of jaundice have occurred from time to time in many parts of the world. These epidemics have remained puzzles, so far as their etiology is concerned, until within the past few years, when, following the reports of researches of a group of Japanese investigators, a microbiologic cause was generally recognized. Even yet, despite the fact of comprehensive reports by Inada and his coworkers, and despite the reports from the battle fields of France, Italy, Germany, and Russia, the facts have not made the proper impression in the United States, except in a small group of workers.

In 1917 Noguchi found that rats captured in New York City were infested with a spirochete apparently identical with that causing spirochetal jaundice in men, and identical with the parasite causing the disease in human beings in Europe and Japan. Jobling made similar observations in Nashville, Tenn., and Neill in Washington. Comprehensive evidence has accumulated to the effect that *Spirocheta icterohemorrhagica* is the cause of a type of jaundice and that the organism is disseminated among the wild rats in various parts of the United States.

As has been shown by Neill, spirochetal jaundice is not a new thing in this country. Quite definite reports of the disease among the troops during the war

*A complete bibliography is given in Neill's article in Public Health Reports, May 10, 1918, pp. 717-726, United States Public Health Service, Washington, D. C.

of 1812 have been found. During the Civil War not less than 71,691 cases were reported among the white troops of the Union Army. Sometimes these cases were sporadic; sometimes they were locally epidemic. While in some instances the cases seemed to be related in some way to malaria, in others the accounts are clear enough to make it almost, if not entirely, certain that the outbreaks were due to the same disease that in later years has been observed in the trenches of European battle fields, but the disease has not been confined to the trenches. It has been reported not infrequently in civil populations.

In all the American reports most of the patients have been described as suffering from nausea or vomiting, some abdominal distress or pain, headache, and fever in varying degrees, followed within a few days by jaundice of different grades in different cases. In fact, says Neill, from many of the descriptions there is little to suggest a specific infectious disease, aside from the fact that a number of cases would appear about the same time in a community which previously and subsequently was free from the disease. Several reports indicate a high mortality among pregnant women. In some outbreaks children seem to have been relatively more frequently attacked than adults, and in others adults were most often subjects of the disease. In some outbreaks males were principally affected, in others the sex incidence was equally divided. In several outbreaks the symptomatology in the fatal cases was strikingly similar and suggestive of rapid necrosis of the liver cells as occurs in acute yellow atrophy.

There is some evidence that direct contact has played a part in transmission.

The starting point of most at least of the outbreaks of infectious jaundice seems to have been the rat, and Noguchi says of this that the finding of the causative agent of infectious jaundice among the wild rats in America, and the identification of this strain with those found in Asia and Europe seems to be particularly important in revealing a latent danger to which we have been constantly exposed, but from which we escape as long as sanitary conditions are not disturbed by untoward events.

Long before the present war acute infectious jaundice was known to occur especially among troops, in sewer workers, in agricultural workers digging in wet soil, and in miners. Persons who handle foods, as butlers and cooks (in Japan at least) are also said to be attacked with especial frequency. While the problem of the rat in relation to this disease has not been completely worked out, the following statement of the mode of transfer forms a reasonable hypothesis: About 10 per cent of all wild rats, wherever located, probably carry the spirochete in their kidneys and excrete them in their urine. If this organism finds a favorable environment in the soil, a sufficient number may live long enough to infect a person who gets them into his mouth or on his skin.

Diagnosis may be made by staining blood films with Romanowsky stains or by one of the impregnation methods; by examination of blood by the dark-field method; and by injection of blood into the peritoneal cavity of a guinea pig. If the spirochetes are present the pig will sicken and die in about ten days, and postmortem will show a combination of hemorrhage and jaundice which is almost pathognomonic. Other methods are microscopic examination of centrifugalized urine sediment stained properly; injection of urine sediment into guinea pigs; and examination of tissues, especially kidney, after staining by the Levaditi method.

—*P. G. W.*

Concerning Medical Manuscripts by Medical Officers

AS stated in the circular memoranda for Editors of Medical Publications issued by the Surgeon General's Office on March 27th and May 22, 1918, it is required by paragraph 423, Manual of the Medical Department, that all medical manuscripts by medical officers, U. S. Army, intended for publication shall be first submitted to the Surgeon General's Office, Washington, D. C., for approval. This regulation, which has been very courteously complied with, to date, is still in force as far as medical officers on active duty are concerned. In the case of medical officers recently retired from active duty, it is requested, as a courtesy to the Surgeon General and in aid of assembling material for the Medical History of the War, that all medical manuscripts based upon military or official records or upon military experience during the War, be submitted as heretofore, to the Secretary, Board of Publications, Surgeon General's Office, Washington, D. C., for record and approval and that such MSS be accompanied by a carbon copy. Upon approval, the original copy will be forwarded to the journal designated, for publication, and the carbon will be filed in the records of the Medical History of the War.

For the Surgeon General:

(Signed) C. R. Darnall, Colonel, Medical Corps,
U. S. A., Executive Officer.

U. S. Interdepartmental Social Hygiene Board

THE United States Interdepartmental Social Hygiene Board, through its Executive Secretary, Dr. T. A. Storey, 1800 Virginia Avenue, N. W., Washington, D. C., announces the following appropriations from the Scientific Research Fund of the Board:

Leland Stanford Junior University Medical School.

(1) "Investigation into more effective treatment in acute and chronic gonorrhea," under the direction of R. L. Rigdon, M.D., Clinical Professor of Genito-urinary Surgery, and A. B. Spalding, M.D., Professor of Obstetrics and Gynecology $2,300

(2) "The permeability of the meninges to anti-syphilitic drugs—an attempt to increase their permeability," under the direction of H. G. Mehrtens, M.D., Clinical Professor of Neurology 2,300

(3) "Investigation into more effective methods of treating syphilis," under the direction of H. E. Alderson, M.D., Clinical Professor of Dermatology 2,600

Total $7,200

University of Michigan, College of Medicine and Surgery.

(1) "A research for an improved method of demonstrating the spirochaeta pallida in human tissues," under the direction of A. S. Warthin, M.D., Professor of Pathology $6,000